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474. *Ion-exchange Studies of Solutions of Arsenites.*

By D. A. Everest and W. J. Popiel.

The sorption of arsenic and of chloride by Amberlite I.R.A-400 (Cl) from arsenious acid solutions has been studied over the pH range 5—13. The results have been interpreted in terms of the sorption of $As_3O_5^-$, $As_2O_4^{2-}$, $H_2AsO_3^-$, $HAsO_3^{2-}$, and AsO_3^{3-}, the actual ion sorbed depending on the pH and the arsenic concentration of the solution studied. Supporting evidence has been obtained from measurement of the ultraviolet absorption spectra of these solutions, and evidence has been obtained that a correlation exists between the ions sorbed by the resin and those present in solution.

The tendency of arsenious acid to undergo condensation in neutral or weakly alkaline solutions was first observed by Auerbach,[1] who investigated 0·03—0·23M-arsenious acid by means of partition experiments between pentyl alcohol and water and by competition experiments between arsenious acid and boric acid for limited quantities of bases. In addition to the presence of simple monoarsenite ions he inferred the presence in more concentrated solutions of diarsenite ions, and possibly some more highly condensed species also. The concentration of condensed arsenious acid species was considered to be low in dilute solution. Garret, Holmes, and Laube [2] determined the solubility of arsenious oxide in sodium hydroxide solution and concluded that the condensed species $HAs_2O_4^-$ and $H_2As_3O_6^-$ were present in the more concentrated arsenious acid solutions.

In other work with more dilute solutions of arsenious acid, formation of condensed arsenite ions could not be detected. Thus Roth and Schwartz,[3] from freezing-point measurements on 0·008—0·06M-arsenious acid, concluded that arsenious acid was entirely in the monomeric form. Similarly Carpeni and Souchay,[4] from pH titrations of arsenious acid solutions up to 0·2M, could obtain no evidence for condensation.

More recently Souchay and Teyssedre [5] repeated and modified the earlier work. They conclude that in 0·2—0·8M-arsenious acid the only condensed species present is $As_3O_5^-$, and that the $HAs_2O_4^-$ ion does not exist or is present in only undetectable quantities. The relative concentration of condensed species does not appear to be very high—in 0·2M-arsenious acid solution only 10% of the arsenic is present as $As_3O_5^-$ ions.[6]

In strongly alkaline solution arsenious acid appears to be always present in the monomeric form, even at relatively high concentrations. Brintzinger and Ratanarat,[7] from dialysis experiments, concluded that arsenious acid was present in strongly alkaline solution as $As(OH)_6^{3-}$. Goldfinger and von Schweinitz [8] observed an absorption line in the ultraviolet absorption spectrum of arsenious acid (up to 0·1M) which they attributed to $H_2AsO_3^-$ ions. On increase in the alkali concentration to 10—12M a second absorption line was obtained which was attributed to the presence of $HAsO_3^{2-}$, and it was considered that these solutions might contain also small amounts of AsO_3^{3-} ions.

The success of ion-exchange methods in the investigation of the condensation of germanic and boric acid [9,10] suggested that similar methods could be used to study condensation of arsenious acid, and its dependence on pH and total arsenic concentration. Preliminary experiments showed that arsenic is sorbed from arsenious acid solutions by the strongly basic ion-exchanger Amberlite I.R.A.-400 in the chloride form.

[1] Auerbach, *Z. anorg. Chem.*, 1903, **37**, 353.
[2] Garret, Holmes, and Laube, *J. Amer. Chem. Soc.*, 1940, **62**, 2024.
[3] Roth and Schwartz, *Ber.*, 1926, **59**, 338.
[4] Carpeni and Souchay, *J. Chim. phys.*, 1945, **42**, 149.
[5] Souchay, *Bull. Soc. chim. France*, 1951, 932; Souchay and Teyssedre, *Compt. rend.*, 1953, **236**, 1965.
[6] Lourijsen-Teyssedre, *Bull. Soc. chim. France*, 1956, 1118.
[7] Brintzinger and Ratanarat, *Z. anorg. Chem.*, 1935, **222**, 317.
[8] Goldfinger and von Schweinitz, *Z. phys. Chem.*, 1932, **19**, 219.
[9] Everest and Salmon, *J.*, 1954, 2438; 1955, 1444.
[10] Everest and Popiel, *J.*, 1956, 3183.

Experimental

Solutions.—Stock solutions, containing *ca.* 0·27 and 0·15 g.-atom of arsenic, were prepared by dissolving " AnalaR " arsenious oxide in the minimum amount of boiling water and diluting it to the required volume.[11] The maximum solubility of arsenious oxide at 25° is stated to be 0·1035 molal,[8] but it was found that more concentrated solutions could be prepared and that they were stable at room temperature for *ca.* 2 days. Portions of these stock solutions (50 ml.) were adjusted to the required pH by addition of sodium hydroxide, and then made up to 75 ml. by addition of water before addition of resin (1·0 g.), thus giving solutions containing 0·18 or 0·10 g.-atom of arsenic per l.

Anion-exchanger.—Amberlite I.R.A.-400 (Cl) (1·0 g.) was used, being prepared from the hydroxide form by treating it with 2N-hydrochloric acid, washing it free from acid and air-drying it before use.

Equilibrium Experiments.—These were carried out as previously described.[10] All wash-water was de-ionised by passage through Permutit " Biodeminrolit " mixed-bed resin.

Analytical Methods.—Arsenic was determined in the filtrate, after separation of the resin phase, by acidification with hydrochloric acid (methyl-red), addition of sodium hydrogen carbonate (*ca.* 1 g.), and titration of arsenic with iodine (starch). Chloride was determined gravimetrically as silver chloride. The quantity " chloride desorbed " from the resin was found from the difference between the total capacity and the chloride loading at equilibrium for any given resin sample.

Measurements of pH were made with a pH meter of commercial type, a glass electrode, and a saturated calomel electrode. For strongly alkaline solutions a Cambridge Instrument Co. " Alki " glass electrode was used.

Ultraviolet Absorption Spectra.—Measurements on arsenious acid solutions were carried out with a Unicam single-beam spectrophotometer. Reference solutions were identical with the test solutions except that arsenic was absent.

Results

The quantity of arsenic sorbed by the resin, the chloride desorbed, and the ratio of g.-atoms of arsenic sorbed to g.-atoms of chloride desorbed (referred to in the discussion as the R value) are represented in Figs. 1 and 2. The R value, which is in effect the average number of arsenic atoms sorbed per " active site " of the resin, is used to determine the number of arsenic atoms present in the actual arsenite ions sorbed.[9, 10] The quantity of arsenic removed from solution did not exceed 12% for either of the arsenic concentrations studied.

The ultraviolet spectrograms obtained show sharp absorption edges, which move to longer wavelengths as the pH of the solution is increased. This bears a close similarity to a colour change in the visible region, as is shown in the chromate–dichromate system, and suggests that a pH-dependent ionic change takes place in solution. The results for solutions containing 0·18 g.-atom of arsenic per l. are given in Fig. 3. Similar observations were recorded for solutions containing 0·1 g.-atom of arsenic per l. although the displacement of the absorption curves was somewhat less marked.

Discussion

Solutions containing 0·18 g.-atom of Arsenic per l.—Maximum sorption of arsenic is found at *ca.* pH 9·2 whereas a maximum in the desorption of chloride occurs at pH 10. As in the ion-exchange investigation of boric acid,[10] this " chloride shift " indicates that as the pH of the arsenious acid solution increases, a transition occurs from the sorption of a univalent condensed ion by the resin to the sorption of a multivalent ion of lower R value. This transition would cause the overall sorption of arsenic to come to a maximum and then to decrease, as is found, since a condensed ionic species is being gradually replaced on the resin by a less condensed one. However, the desorption of chloride ions will continue since a univalent ion is being replaced on the resin by a multivalent one. In this way the desorption of chloride ions comes to a peak at a higher pH value than that at which the maximum in the arsenic sorption occurs.

[11] Margulis and Ganc, *Ann. Agron.*, 1947, **17**, 568.

The sorption of a mixture of $As_3O_5^-$ (R 3)[2,6] and $As_2O_4^{2-}$ (R 1) in the pH region 5—9 would explain our results, the equilibrium in solution between these ions changing in favour of $As_2O_4^{2-}$ as the pH increases, thus explaining the decrease in the value of R from *ca.* 2·8—2·5 down to 1 (Fig. 1). The multivalent species reaches a maximum concentration

FIG. 1.

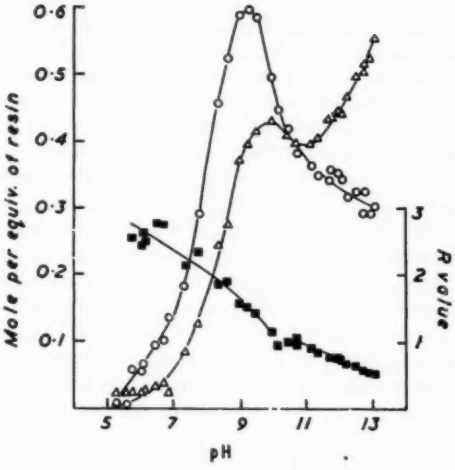
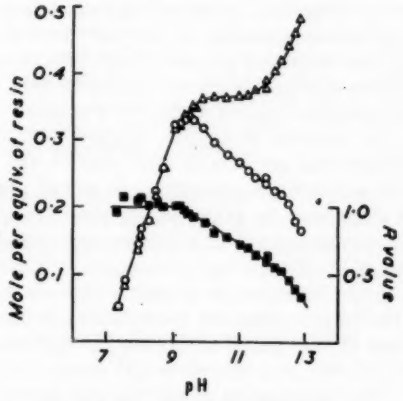


FIG. 2.



FIGS. 1 *and* 2. *Sorption of arsenic and chloride by resin* I.R.A.-400 (Cl) (1·0 *g.*). *Concn.* (*g.-atom per l.*) *of* As *in soln.*: *Fig.* 1, 0·18; *Fig.* 2, 0·1. ○ *Sorption of* As, *and* △ *desorption of* Cl *by resin* (1 *g.*). ■ *R value.*

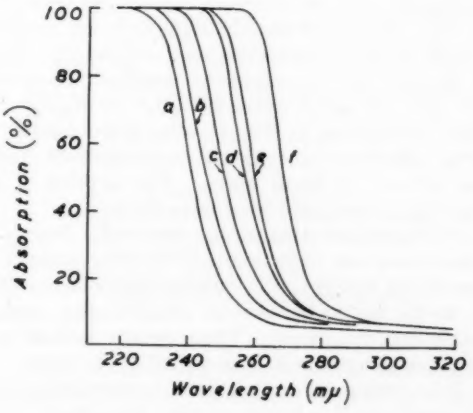


FIG. 3. *Absorption spectrograms* (1 *cm. cells*) *of* 0·18 *g.-atom of arsenic at* pH: *a*, 5·0; *b*, 7·42; *c*, 8·02; *d*, 8·88; *e*, 11·46; *f*, 12·10.

near the peak of the chloride desorption (pH 10), and it is significant that the values of R in this region of pH closely approach unity. But whereas the value of R remains steadily at unity in the pH region 10—11, the desorption of chloride ion decreases, which implies a further change from $As_2O_4^{2-}$ to $H_2AsO_3^-$ (both of R 1).

Above pH 11 the chloride-desorption curve rises steadily, whereas the arsenic sorption curve falls and flattens out, whilst the R values tend towards 0·5. This implies that at

higher pH values the species $HAsO_3^{2-}$ is being sorbed, and is in agreement with the observations of Goldfinger and von Schweinitz.[8]

Solutions containing 0·1 *g.-atom of Arsenic per l.*—A maximum R value of unity is maintained in the pH region 7—9·5 (Fig. 2), which indicates sorption of $As_2O_4^{2-}$ or $H_2AsO_3^-$ ions. Although the presence of monoarsenite ions only in this concentration range would be in agreement with the results of other workers,[3,4,5] our spectrophotometric studies indicate a large displacement of the absorption edges in the pH region 7—9, suggesting a marked ionic change in solution. This implies a transition from $As_2O_4^{2-}$ to $H_2AsO_3^-$ in this range. The chloride-desorption curve shows a point of inflection in the pH range 10—11 (Fig. 2), corresponding to a steady decrease in the value of R. This indicates the progressive formation of $HAsO_3^{2-}$ ions in solution (R 0·5), the tendency for sorption of this ion becoming greater at pH 11·5 as is shown by the sudden increase in slope of the chloride-desorption curve. At pH 12·5 the R value of 0·5 shows that the $HAsO_3^{2-}$ ion is then the principal species sorbed by the resin. Above this pH value there is a rapid decrease in the sorption of arsenic, coupled with an increase in the desorption of chloride. This suggests the sorption of OH^- ions by the resin, the concentration of which in solution is now becoming appreciable. It is not precluded however that a species such as AsO_3^{3-} (R 0·33) may be taken up by the resin in this pH region. The existence of this ion in solution above pH 12 has been suggested by the work of Goldfinger and von Schweinitz [8] and of Brintzinger and Ratanarat.[7] That the sorption of the hydroxyl ion is not as great as might be expected at such a high alkalinity is shown by the fact that, although at pH $<$12 the pH values of the equilibrium solutions were found to be consistently lower than those of the initial solutions, nevertheless this discrepancy was never greater than *ca.* 0·2 pH unit over the whole pH range studied.

Our formulation of the various arsenite ions occurring in arsenious acid solutions is consistent with the results obtained by Nelson [12] for the As_2O_3–Na_2O–H_2O system. He found the following arsenites to be formed: $Na_2O,3As_2O_3$ ($Na_2As_6O_{10}$); Na_2O,As_2O_3 ($Na_2As_2O_4$); $2Na_2O,As_2O_3,7H_2O$ ($Na_4As_2O_5,7H_2O$); $2Na_2O,As_2O_3$ ($Na_4As_2O_5$). The first two compounds can be considered to contain $As_3O_5^-$ and $As_2O_4^{2-}$ ions respectively. The last two can be considered as derived from the $H_2As_2O_5^{2-}$ ion by the replacement of the two hydrogen atoms, the $H_2As_2O_5^{2-}$ ion being simply the hydrated form of $As_2O_4^{2-}$.

The sorption of a species such as $HAs_3O_6^{2-}$ (R 1·5), instead of the $As_2O_4^{2-}$ ion, might on our evidence be considered possible. From the previous discussion of the chloride shift the sorption of either $HAs_3O_6^{2-}$ or $As_2O_4^{2-}$ ions by the resin would be expected to reach a maximum at the pH value corresponding to the peak in the chloride-desorption curve. However, at both the concentrations studied, the value of R at this point has been on or just below unity. The sorption of $As_2O_4^{2-}$ ions by the resin rather than $HAs_3O_6^{2-}$ is thus considered more likely.

It is significant that, in the ultraviolet absorption studies, the maximum displacement of the absorption edges occurs in the pH regions at which our ion-exchange results indicate a maximum change in the ionic species sorbed by the resin (*i.e.*, at *ca.* pH 7—9·5 and above pH 11 for the higher arsenic concentration, and pH 7—9 and above 12 for the lower arsenic concentrations). These results indicate a definite correlation between the ions present in solution and those sorbed by the resin.

It is worth mention that similar spectrograms to ours have been observed with solutions of telluric acid,[13] indicating similar behaviour.

BATTERSEA POLYTECHNIC, LONDON, S.W.11. [*Received, November* 14*th*, 1956.]

[12] Nelson, *J. Amer. Chem. Soc.*, 1941, **63**, 1870.
[13] Scott and Leonard, *Analyt. Chem.*, 1954, **26**, 445; Stüber, Braida, and Jander, *Z. phys. Chem.*, 1934, **171**, *A*, 320.

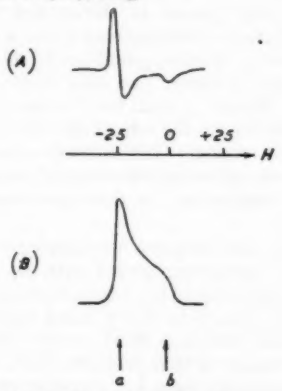
475. *Solutions of Sulphur in Oleum. Part I. Electron-spin Resonance of Solutions of Sulphur in Oleum.*

By D. J. E. Ingram and M. C. R. Symons.

Blue solutions of sulphur in concentrated oleum, although diamagnetic by conventional susceptibility measurements, show a strong electron-spin resonance absorption and must therefore contain a little of some species having unpaired electrons. At 90° K the absorption curve has a sharp peak with a *g*-value of 2·018 and a shoulder having a *g*-value of 2·003. Measurements at two different wavelengths show that this asymmetry is due to a variation in the *g*-value and is not a fine or hyperfine structure. On addition of aqueous sulphuric acid to the solution this line diminishes in intensity and a new line appears having a peak and shoulder with *g*-values of 2·025 and 2·032, respectively. It is postulated that this second line is caused by polymeric sulphur radicals similar to those present in liquid sulphur.

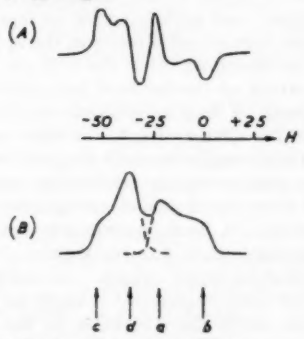
It has been stated [1] that the cause of the colour in blue solutions formed by dissolving sulphur or iodine in oleum is sulphur sesquioxide, and this work was undertaken to investigate this statement. The postulate that blue iodine solutions contain free iodine

Fig. 1. *Absorption line obtained from a solution of sulphur in concentrated oleum* (65% SO_3).



(*A*) Derivative as traced out.
(*B*) Reconstructed absorption with *g*-values: $a \equiv 2{\cdot}018$, $b \equiv 2{\cdot}003$.
Magnetic field strengths are quoted in gauss centred on the free-spin value.

Fig. 2. *Absorption line obtained from a solution of sulphur in dilute oleum* (20% SO_3).



(*A*) Derivative as traced out.
(*B*) Reconstructed absorption with *g*-values: $a \equiv 2{\cdot}018$, $b \equiv 2{\cdot}003$, $c \equiv 2{\cdot}032$, $d \equiv 2{\cdot}025$.
Magnetic field strengths are quoted in gauss centred on the free-spin value.

cations [2] is based largely on the observation that the solutions contain a paramagnetic species in large concentration. This paramagnetic species, which was detected by conventional magnetic-susceptibility measurements, does not give an observable electron-resonance absorption at 90° K, presumably because the absorption is too broad at this temperature, or because there is a large zero-field splitting of the triplet levels. In contrast, blue solutions of sulphur, which are found by susceptibility measurements to contain no bulk paramagnetic component,[3] have a strong electron-resonance absorption,

[1] Masson and Argument, *J.*, 1938, 1705.
[2] Symons, *J.*, 1957, 387, 2186.
[3] Symons, following paper.

and therefore contain some species with unpaired electrons in such low concentrations that it cannot be detected satisfactorily by conventional methods.

When these solutions are treated with aqueous sulphuric acid the colour changes from blue, *via* green, to brown, and ultimately sulphur is precipitated. During this process the strong resonance absorption characteristic of the blue solution rapidly decreases and loses its well-defined peak, and a new, weak absorption line appears at a slightly lower field strength. Both bands vanish when sulphur is precipitated.

Typical results obtained from blue and brown solutions are shown in Figs. 1 and 2, respectively. In each case (*A*) represents the derivative of the absorption curve and (*B*) an integrated reconstruction of the actual absorption curve. These curves were obtained from solutions at 90° K. When the brown solutions were allowed to warm the two bands changed markedly as soon as the glassy solvent became fluid. The shoulders of both lines vanished leaving two narrow lines. The brief reference made by Gardner and Fraenkel to the detection of two radicals in solutions of sulphur in oleum probably relates to these narrow, symmetrical lines.[4]

Experimental

Sulphuric acid and oleums were purified as described earlier,[2] and their purity checked by spectrophotometric measurements in the 200—300 mμ range with a Unicam SP500 spectrophotometer. Oleum strengths were estimated by the "fog–clear" method described by Kunzler.[5] Sulphur was purified by the procedure of Bacon and Fanelli.[6] Samples for measurement in the 3 cm. wavelength spectrometer were placed in thin-walled test tubes (3 mm. diam.) and rapidly cooled in liquid oxygen so that a homogeneous glass was formed. These tubes were placed directly in the apparatus. Since only small quantities of solution were required for measurement in the 1·25 cm. wavelength spectrometer, and since it was necessary to avoid attack on the inside of the cavity by sulphur trioxide vapour, the following procedure was adopted. A thin mica sheet was stuck to the bottom of the adjustable short-circuiting plunger of the cavity, which was then cooled in liquid oxygen. Immediately after removal from the liquid oxygen a small drop of oleum solution was placed in the centre of the mica, and the cavity plunger rapidly screwed into position in the apparatus. In this way it was possible to re-cool before the frozen oleum became fluid.

Apparatus.—A 3-cm. wavelength electron resonance spectroscope was employed for most of the measurements, the rectangular H_{012} resonator being surrounded with an evacuated jacket containing liquid oxygen. In order to obtain a high sensitivity, phase-sensitive methods of detection were employed,[7] a small amplitude 100 kc./sec. field sweep being applied across the sample, while the d.c. value of the main magnetic field was slowly swept through the resonance value. The output from the phase-sensitive mixer is thus proportional to the derivative of the absorption line, and it is passed to a pen-recorder *via* a d.c. amplifier chain. The electron resonance spectrum is thus continuously recorded, and two examples of observed spectra are shown in Figs. 1*A* and 2*A* together with the calculated *g*-values. The horizontal axes of these figures thus correspond to changing value of d.c. magnetic field, while the magnitude of the deflection parallel to the vertical axis is equal to the derivative of the absorption line at that point. A maximum in this trace therefore corresponds to a point of maximum slope on the actual absorption curve, while an intercept with the axis indicates a point of inflexion on the absorption line. The actual shape of the resonance absorption can therefore be deduced from the derivatives, and such are reconstructed in Figs. 1*B* and 2*B*. Fig. 1 is for solutions containing a high concentration of SO_3 (65%), while Fig. 2 is for a solution containing the same amount of sulphur (*ca.* 0·1M) but less SO_3 (20%).

The determination of the resonance field strengths and *g*-values (for definition see ref. 8)

[4] Gardner and Fraenkel, *J. Amer. Chem. Soc.*, 1956, **78**, 3279.
[5] Kunzler, *Analyt. Chem.*, 1953, **25**, 193.
[6] Bacon and Fanelli, *Ind. Eng. Chem.*, 1942, **34**, 1043.
[7] Ingram, "Spectroscopy at Radio and Microwave Frequencies," Butterworths, 1955, p. 35.
[8] Ingram, *ibid.*, pp. 142 and 66.

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was effected by affixing a small amount of free-radical marker, αα-diphenyl-β-picrylhydrazyl, to the specimen tube and observing the superimposed spectra. The sharp peak was found to fall on the high-field edge of the main absorption line as indicated in Fig. 1*B*. The *g*-values corresponding to the other peaks could then be calculated directly from the measured field increments.

Some measurements were also made at 1·25 cm. wavelengths at liquid-air temperatures, by use of a standard H_{111} low-temperature cavity.[8] These were performed to check whether the asymmetry of the line shape was due to an anisotropic *g*-value or a zero-field electronic splitting of triplet state levels. The former would give a line width which increased with increasing frequency of observation, whereas the line width would remain constant if due to the latter effect. In fact it was found that a large increase in width was obtained at the higher frequencies, indicating that the shape of the main absorption curve is due to an anisotropic *g*-value. Unfortunately this test could not be applied to the second band because the methods used for detection were less sensitive and the shoulder was not observable with 1·25 cm. radiation. However the fact that both bands changed to single narrow lines when the glass softened suggests that this asymmetry is also due to variation of the *g*-value, since this effect is characteristic of anisotropic transitions when the medium changes from being rigid to fluid.[9]

Discussion

Since one absorption band increases when the other decreases they must be caused by two different radicals and cannot be two transitions of a single species with two unpaired electrons. Gardner and Fraenkel[4] have not observed a *g*-value variation for any of the sulphur radicals studied and they state that anisotropic contributions are unlikely: their failure to observe it in oleum solutions may be because they used fluid solutions.

The high *g*-value of about 2·02 shows that spin–orbit coupling must be appreciable, and, as suggested by Gardner and Fraenkel, may be characteristic of free radicals in which the odd electron is located primarily on sulphur.

These radicals form only a very small component of solutions whose bulk composition is uncertain, and therefore precise identification is impossible. However, the second line appears just before the solid sulphur separates, and since the polymeric radicals present in liquid sulphur have a *g*-value of 2·024,[4] it is suggested that this same radical may be formed as a precursor to the formation of solid sulphur.

The distinction between the sulphur and iodine solutions is clear, the former having no major paramagnetic content but one or two radical species in small concentration readily detectable by their electron-resonance absorption, the latter containing large concentrations of a paramagnetic species which, however, is not detectable by electron resonance techniques at 90° K.

The University, Southampton. [*Received, December 3rd*, 1956.]

[9] Bennett, Ingram, and Schonland, *Proc. Phys. Soc.*, 1956, *A*, **69**, 556.

476. *Solutions of Sulphur in Oleum. Part II.* Visible and Ultraviolet Absorption Spectra.*

By M. C. R. Symons.

Spectra of freshly prepared, blue solutions of sulphur in concentrated oleum show absorption bands with maxima at 590 and 335 mμ, but on storage the latter slowly increases in intensity at the expense of the former. At ~50° this effect is reversed. A reversible equilibrium between monomeric and polymeric sulphur sesquioxide is postulated to explain these changes, high temperature favouring the monomer. Corresponding changes in magnetic susceptibility show that, after warming, there is a marked increase in the concentration of some paramagnetic species, and the nature of this species is discussed.

Whilst the green-blue solid which is precipitated when sulphur trioxide and sulphur interact has been studied extensively [1-4] and shown to be sulphur sesquioxide with the empirical formula S_2O_3, little attention has been paid to the deep blue, homogeneous solutions formed when sulphur or the sesquioxide is dissolved in concentrated oleum. Partington and Vogel [1] established that these solutions, in contrast with the green or brown solutions obtained when the concentration of sulphur trioxide is small, are not colloidal, and naturally assumed that they are simply solutions of the sesquioxide; they state that the solutions are very unstable.

The colour of the sesquioxide is always described as green-blue, although Wohler and Wegwitz [2] found that when excess of sulphur trioxide was removed, the residual solid was brown. In contrast, the solutions are deep blue owing, as can be seen from curve *a* in Fig. 1, to a band at 590 mμ. Since these solutions contain an unidentified paramagnetic substance [5] in low concentration their electronic absorption spectra and magnetic susceptibilities have been studied. Although the concentration of paramagnetic material is too small for conclusive detection by the Gouy technique because of unascertainable diamagnetic corrections, the results reported in Part I [5] show that in concentrated solutions it should contribute a pull of several milligrams to the overall change in weight and hence any change in concentration of the paramagnetic species, unaccompanied by large changes in the bulk composition of the solution, should be readily detectable.

The results are summarised in Figs. 1 and 2. Two spectral effects may be distinguished; treating a blue solution with sulphuric acid so that the concentration of sulphur trioxide is lowered, changes the colour from blue to brown, and later sulphur is precipitated. Vogel and Partington [1] established that the brown solutions are colloidal, and the spectrum (curve *c*) is characteristic of such a solution. Also, the spectra of fresh solutions (curve *a*) containing a large concentration of sulphur trioxide change with time, the intensity of the peak at 590 mμ slowly decreasing, with a corresponding increase in that of the 335 mμ band, until after several days (curve *b*) dilute solutions appear colourless. If the solution is then warmed to about 50°, an intense blue colour slowly develops and is retained on cooling. The spectrum of the resulting solution is similar to that of the original solution (curve *a*), and again changes with time in an identical manner. With care, very little sulphur dioxide is evolved during this cycle, and a colourless solution, kept at room temperature for many weeks, still assumes an intense blue colour on warming. However,

* Part I, preceding paper.

[1] Vogel and Partington, *J.*, 1925, 1514.
[2] Wöhler and Wegwitz, *Z. anorg. Chem.*, 1933, **213**, 129.
[3] Appel, *Naturwiss.*, 1953, **40**, 509.
[4] Murthy, *Nature*, 1951, **168**, 475.
[5] Ingram and Symons, preceding paper.

overheating causes vigorous evolution of sulphur dioxide and total loss of both bands (curve *d*).

Magnetic-susceptibility measurements showed an apparent increase in the overall diamagnetism of the solutions corresponding with the decay in the 590 mμ peak (Fig. 2). Since the susceptibility of the aged solutions was nearly the same as that of the pure solvent and of the residual solvent after total decomposition of the solute by heat, it is concluded that the decrease in diamagnetism found immediately after the restoration of the blue colour is caused by the presence of a paramagnetic substance.

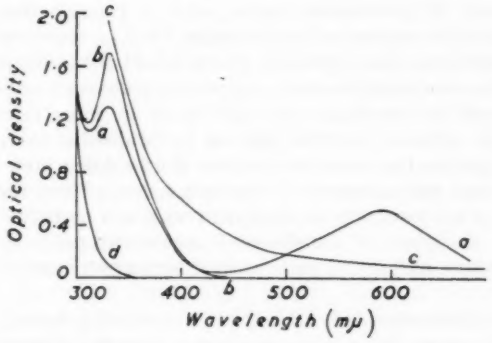
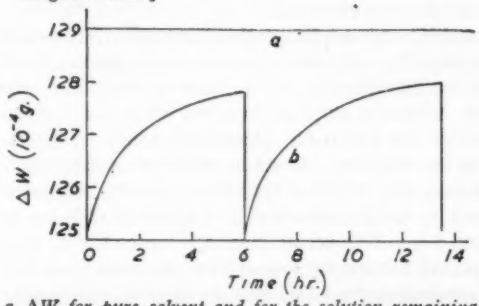


FIG. 1. *Absorption spectra of solutions of sulphur in oleum.*

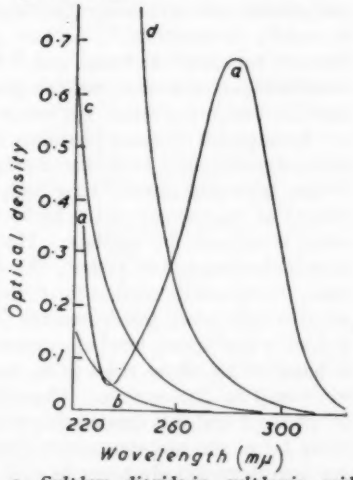
a, Freshly prepared solution in concentrated oleum (65%). *b, Same solution after 24 hours. d, Same solution after prolonged heating. c, Solution of sulphur in dilute oleum* (10%).

FIG. 2. *Effect of heat on the magnetic susceptibility of a solution of sulphur in oleum* (65%). [ΔW is the difference between the weight of the tube and its contents in the presence and in the absence of the magnetic field.]



a, ΔW *for pure solvent and for the solution remaining after thermal decomposition of the sulphur sesquioxide. b, Variation in* ΔW *with time of a freshly prepared solution, and the effect of heat on* ΔW. *All readings were made at the same temperature. The readings obtained 6 and 13·5 hours after preparation were made as soon as possible after warming.*

FIG. 3. *Absorption spectra of various oleums and of sulphur dioxide in sulphuric acid.*



a, Sulphur dioxide in sulphuric acid (98·4%). *b,* 34% *Oleum. c,* 40% *Oleum. d,* 60% *Oleum.*

The simplest inference is that the blue compound is paramagnetic. A rough estimation of the radical concentration shows that, on this assumption, the extinction coefficient at 590 mμ lies between 10^3 and 10^4, showing that the transition is a permitted one. It is equally reasonable to postulate that the concentration of the paramagnetic species is directly dependent upon the concentration of the blue compound, or even that they are produced by two completely separate processes when the solution is heated. There is insufficient evidence available for an unequivocal conclusion, but certain alternative interpretations seem sufficiently well founded to warrant discussion.

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Discussion

It has been concluded that two distinct radical species may occur in solutions of sulphur in oleum, one being favoured by high and the other by low concentrations of sulphur trioxide.[5] These two radicals will be considered in turn. When the oleum is dilute the solutions are colloidal,[1] and precipitation of the sulphur is probably prevented because the solvent is able to protonate S_x molecules. If protonation can occur it is possible that polymeric diradicals, such as are thought to be present in liquid sulphur,[6] will be stabilised by protonation near the ends of the molecules, since repulsive effects would then inhibit cyclisation. These diradicals will behave essentially as two separate radicals since conjugation through the sulphur chain would be impossible provided there are more than three atoms in the chain. However, the unpaired electron will not be localised entirely on the end sulphur atom and may be in part on the second or even the third sulphur atom. Thus the structure resembles in some ways the superoxide or ozonide systems,[7] and the observation of an ill-defined variation [5] in the *g*-value is in agreement with this postulate. (The *g*-value is a measure of the rate of divergence of the electronic levels with magnetic field, and a spread in the electron resonance absorption curve caused by magnetic anisotropy is known as a *g*-value variation.)

These radicals are destroyed when sulphur trioxide is added, but a new one is formed in very much greater concentration. This time, the *g*-value variation is very well defined and spread over a considerable range. There can be little doubt therefore that the radical is axially symmetrical.[8] Certain possibilities arise. In several, the radical considered has two unpaired electrons, and it has already been stressed [5] that such species are somewhat less probable than radicals possessing only one electron or in which one is effectively insulated from the other, since only one transition is observed.

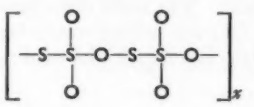
Perhaps the simplest postulate is that monomeric sulphur sesquioxide is both blue and paramagnetic, and that this slowly disappears by polymerisation at room temperature. It has been postulated [9] that S_2O_3 should be diamagnetic, in contrast to SO_4, since the three-fold degeneracy of the highest-energy orbital of sulphate is lifted when one oxygen atom is replaced by sulphur. This argument was based on calculations made by Helmholz, Brennan, and Wolfsberg [10] relating to the electronic structure of the fluorochromate ion. They concluded that the three-fold degenerate orbital of the chromate ion (designated as t_1) is split when the symmetry is reduced by the introduction of fluorine or chlorine to a doubly degenerate level of symmetry e and a non-degenerate level a_2. Since the a_2 level is found to lie above the e level, the compound formed by loss of two electrons from this ion would be diamagnetic. However, extrapolation from this case to sulphur sesquioxide is not short and it is conceivable that these levels are inverted, the doubly degenerate level lying below the non-degenerate level in the S_2O_3 molecule. This would mean that there are two unpaired electrons in S_2O_3, which could therefore possibly be the paramagnetic species in question. This radical has axial symmetry as required by the electron-resonance spectrum.

It has been reported that the monomeric compound SO_4 is colourless in solution.[11] This is in accord with the scheme proposed by Wolfsberg and Helmholz [12] for the perchlorate ion, since the first permitted electronic transition of an ion formed by the loss of two electrons would be $(t_1)^4 \longrightarrow (t_1)^3(3t_2)$ which would be of great energy. However in the S_2O_3 molecule, transition between the e and the a_2 level would be allowed, and hence there should be an intense absorption band of relatively low energy. This is in accord with

[6] Gardner and Fraenkel, *J. Amer. Chem. Soc.*, 1956, **78**, 3279.
[7] Bennett, Ingram, Symons, George, and Griffiths, *Phil. Mag.*, 1955, **46**, 443.
[8] Sands, *Phys. Rev.*, 1955, **99**, 1222.
[9] Symons, *J.*, 1957, 387.
[10] Helmholz, Brennan, and Wolfsberg, *J. Chem. Phys.*, 1955, **23**, 853.
[11] Schwarz and Achenbach, *Z. anorg. Chem.*, 1934, **219**, 271.
[12] Wolfsberg and Helmholz, *J. Chem. Phys.*, 1952, **20**, 837.

the postulate that the band at 590 mμ is caused by monomeric sulphur sesquioxide and that the molar extinction coefficient is between 10^3 and 10^4.

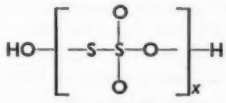
If this concept is correct, the slow decrease in colour and paramagnetism could be interpreted as a polymerisation process $xS_2O_3 \longrightarrow (S_2O_3)_x$. The new band at 335 mμ would then be ascribed to the polymer, which probably has the symmetrical "head to tail" structure (*A*) analogous to that of polymeric sulphur trioxide. Evidence for this structure is provided by Appel's work.[3] Each unit within the polymer is structurally analogous to a disubstituted sulphate ion. Thus the situation resembles that discussed by Helmholz *et al.*,[10] and the fact [13] that the first electronic transition for sulphonyl chloride is at 303 mμ is in accord with this picture. At high concentrations the edge of the 335 mμ band would extend into the visible region, causing the polymer to appear yellow or brown. However, surface decomposition caused by moisture would involve the formation of monomer as in solution, and hence the solid might appear green.



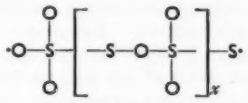
(*A*)

Recently Brayford and Wyatt [14] concluded, on the basis of cryoscopic measurements, that sulphur dissolved in oleum (45%) is present largely as sulphur sesquioxide. They observed a slow increase in the measured *i*-factor before a constant value was obtained, and attributed this to either the slow dissolution of sulphur or a slow conversion of colloidal sulphur into the sesquioxide. If either interpretation is correct the phenomenon is not related to the changes described here. Brayford and Wyatt state that the sulphur sesquioxide may not be entirely monomeric.

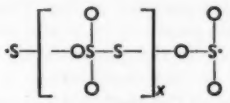
A consideration of the nature of the end groups in such a polymer leads to an alternative theory. In polymeric sulphur trioxide the end groups are almost certainly H and OH, and the polymerisation, which is catalysed by traces of water,[15] must be ionic in type. However, polymeric sulphur appears to be formed by a radical process, the ends of each molecule being neutral radicals. Since polymeric sulphur sesquioxide is half-way between these extremes either type of polymer seems reasonable. By analogy with sulphur



(*B*)



(*C*)



(*D*)

trioxide one could formulate the polymer as (*B*) or, by analogy with sulphur, as (*C*) or (*D*). There are at least four alternative end groups for such polymeric radicals, each of which would be expected to have a characteristic electron-resonance absorption spectrum. It is conceivable that two radical structures are more stable than the remainder, and that their structural similarities are such that the electron-spin resonance spectra merge to give the curve recorded in Part I.[5]

Two further possibilities exist, namely, that the paramagnetic species is monomeric sulphur monoxide or the diradical HS^+. Both have axial symmetry and probably two unpaired electrons. Evidence that sulphur monoxide is one of the decomposition products of solid sulphur sesquioxide has been presented by Murthy.[4] Both monomer and dimer have absorption maxima in the 320 mμ region but no transition in the visible region. It is conceivable therefore that the band at 335 mμ is caused by sulphur monoxide, but in that case, since the paramagnetism decreases as this band increases, the monoxide would have to be present in the dimeric form.[16]

The formation of the radical HS^+ is postulated because of the similarities between this

[13] Thompson, *Nature*, 1933, **132**, 896.
[14] Brayford and Wyatt, *Trans. Faraday Soc.*, 1956, **52**, 642.
[15] Bigeon, *Ind. chim.*, 1953, **40**, 106.
[16] Jones, *J. Chem. Phys.*, 1950, **18**, 1263.

system and that of iodine in oleum.[9] The iodine cation, thought to be present in the latter solution, could react with sulphur trioxide to form ISO_3^+.[9] The analogous equilibrium $S_2O_3 \rightleftharpoons SO_3 + S$ is far less probable, not only because iodine cations are intrinsically more probable than free sulphur atoms, but also because the former will be stabilised by solvation, whilst sulphur atoms would immediately combine to form solid sulphur. However, if the sesquioxide were capable of accepting a proton to form $HS_2O_3^+$, then this might reversibly dissociate to form HS^+ in very low concentration. The main objection to this theory is that interaction between the unpaired electrons and the proton would be expected and should manifest itself as a splitting of the magnetic resonance line into a doublet which has not been detected.

Experimental

Materials were purified, and solutions prepared as described in Part I.[6] Because of the difficulties involved in the preparation of pure sulphur the following alternative procedure was used in addition to that already described. "AnalaR" sodium thiosulphate was dissolved in concentrated sulphuric acid. The resulting suspension was warmed to expel sulphur dioxide, and sulphur trioxide was added as required. The results were identical with those obtained from solutions prepared from the element.

Spectroscopic measurements were made with a Unicam S.P.600 glass spectrophotometer, and a Unicam S.P.500 quartz spectrophotometer. Calibrated quartz cells of 1 mm. and 1 cm. thickness were used, the latter equipped with stoppers. The 1 mm. cells were not covered since absorption of small amounts of water on the surface of the solution resulted in the formation of an upper layer which effectively sealed the solution from the atmosphere. The spectra recorded in Figs. 1 and 2 were measured against pure solvent as a control material. Measurements were usually made down to 220 mμ and in every case a pronounced peak at 280 mμ was found. This was almost certainly caused by dissolved sulphur dioxide, which is fairly soluble in sulphuric acid. The spectrum of a solution of sulphur dioxide in sulphuric acid is recorded in Fig. 3, curve *a*.

Also recorded in Fig. 3 are the absorption spectra for oleums of various strengths measured against pure sulphuric acid as control material. By comparison with the spectrum for sulphur trioxide in the gaseous state [17] it may be seen that the concentration of free sulphur trioxide must be very small indeed in dilute oleum,[18] but that as the percentage of sulphur trioxide is increased the absorption at low wavelengths increases very rapidly, as does the vapour pressure of the solutions;[19] and it seems probable that this increased absorption is caused by free sulphur trioxide.[14]

Magnetic measurements were made with a conventional Gouy balance at room temperature, as described earlier.[9] The results are recorded in Fig. 2.

Thanks are offered to Dr. D. Schonland for helpful advice.

The University, Southampton. [*Received, December 20th*, 1956.]

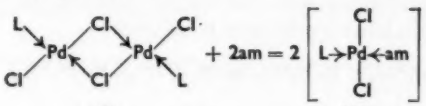
[17] Fajans and Goodeve, *Trans. Faraday Soc.*, 1936, **32**, 511.
[18] Gillespie, *J.*, 1950, 2493.
[19] Yost and Russell, "Systematic Inorganic Chemistry," Prentice-Hall Inc., New York, 1944, p. 340.

477. *The Reaction of Monoamines with Chloro-bridged Complexes of Palladium*(II).

By J. Chatt and L. M. Venanzi.

Most chloro-bridged complexes of the type $L_2Pd_2Cl_4$ (I) react with monoamines, am, as follows: $[L_2Pd_2Cl_4] + 2am \rightleftharpoons 2[L,amPdCl_2]$ (II), but the product (II) can be isolated only when the donor atom in the ligand L is phosphorus and arsenic. When the donor atom is sulphur, selenium, or tellurium, the mixed product disproportionates measurably slowly in solution at room temperature: $2[L,amPdCl_2] \longrightarrow [L_2PdCl_2] + [am_2PdCl_2]$. When L is an olefin, immediate decomposition of the product occurs even at $-70°$. When the halogen is iodine the equilibrium lies so far to the side of the bridged complex that the mixed product can be isolated, if at all, only in the presence of a large excess of the amine.

The reaction of amines with the halogen-bridged complexes of palladium, $[L_2Pd_2Cl_4]$ (I), containing tertiary phosphines and arsines as ligands L has been studied by Mann and his co-workers.[1] They showed that the following reaction occurs almost instantaneously in organic solvents at room temperature:



(I) (II)

We needed compounds such as (II) with a large variety of ligands L to further our study of inductive and mesomeric effects in complex compounds,[2] so we attempted to obtain them by this reaction from the bridged compounds previously described.[3] However, the only mixed complexes which we could isolate were those containing phosphorus and arsenic as donor atoms in the ligands L, and new compounds of this type are listed in the Table.

Complex	M. p.	Colour
PEt_3,piperidinePdCl$_2$	73·5—75°	Orange-yellow
PPr^n_3,piperidinePdCl$_2$	116—118	Orange-yellow
PBu^n_2Ph,piperidinePdCl$_2$	64—64·5	Orange-yellow
PPh_3,piperidinePdCl$_2$	160—172 (decomp.)	Yellow-orange
$P(MeO)_3$,piperidinePdCl$_2$	90—91	Orange-yellow
$P(PhO)_3$,piperidinePdCl$_2$	131—132	Orange-yellow
$AsEt_3$,piperidinePdCl$_2$	68—70	Yellow-orange
PPr^n_3,*p*-toluidinePdCl$_2$	91·5—92·5	Yellow-orange
PBu^n_2Ph,*p*-toluidinePdCl$_2$	111·5—113	Yellow-orange
PPh_3,*p*-toluidinePdCl$_2$,MeOH	218 (decomp.)	Dark orange
PPh_3,*p*-toluidinePdCl$_2$,EtOH	218—220 (decomp.)	Dark orange
PPh_3,*p*-toluidinePdCl$_2$,PrOH	200—220 (decomp.)	Orange
$P(MeO)_3$,*p*-toluidinePdCl$_2$	131—131·5	Yellow-orange
$P(PhO)_3$,*p*-toluidinePdCl$_2$	115·5—116·5	Yellow-orange
PPr^n_3,*p*-toluidinePdI$_2$	107	Red

Finck[4] obtained two mixed phosphite–*p*-toluidine complexes, $[P(MeO)_3$,*p*-toluidine-$PdCl_2]$ and $[P(EtO)_3$,*p*-toluidine$PdCl_2]$, by reaction of an excess of *p*-toluidine with $[\{P(MeO)_3\}_2PdCl_2]$ and $[\{P(EtO)_3\}_2PdCl_2]$ respectively. He describes them as white solids. The compounds of that type which we have obtained are orange-yellow and certainly have a *trans*-configuration. If Finck's compounds have the formula claimed, it seems that they might have *cis*-configurations, and the mixed phosphite–*p*-toluidine

[1] Mann, *Ann. Reports*, 1938, **35**, 148; Chatt and Mann, *J.*, 1939, 1622.
[2] Chatt, Duncanson, and Venanzi, *J.*, 1955, 4461.
[3] Chatt and Venanzi, *J.*, 1957, 2351.
[4] Finck, *Compt. rend.*, 1896, **123**, 603.

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complexes could thus provide another example of non-labile geometrical isomerism, which is very rare in the palladous series of complexes.

Mixed complexes of the type *trans*-[L,amPdCl$_2$], containing donor atoms from Group VI, are formed by the reaction of amines with the appropriate bridged complex [(R$_2$M)$_2$Pd$_2$Cl$_4$] (M = S, Se, or Te), but they disproportionate spontaneously into (R$_2$M)$_2$PdCl$_2$ and am$_2$PdCl$_2$ at room temperature, and could not be isolated:

$$[(Et_2Te)_2Pd_2Cl_4] + 2Piperidine \longrightarrow 2[Et_2Te,piperidinePdCl_2]$$

$$2[Et_2Te,piperidinePdCl_2] \longrightarrow [(Et_2Te)_2PdCl_2] + [(piperidine)_2PdCl_2]$$

This disproportionation was evident from the infrared spectrum of a solution of the freshly mixed components. For example, a freshly prepared solution of [(Et$_2$Te)$_2$Pd$_2$Cl$_4$] and piperidine (1 : 2) in carbon tetrachloride has an absorption band at 3249 cm.$^{-1}$ attributable to the N–H stretching vibration of the complex, [Et$_2$Te,piperidinePdCl$_2$], but this band gradually decreases in intensity while a second band appears at 3237 cm.$^{-1}$ corresponding to the N–H stretching vibration of the complex [(piperidine)$_2$PdCl$_2$].

The reaction of *p*-toluidine with the bridged olefin complex [(*cyclo*hexene)$_2$Pd$_2$Cl$_4$] in methylene chloride at −70° led to the immediate decomposition of the complex.[3]

Attempts to obtain mixed amine complexes, [am,am'PdCl$_2$], were unsuccessful.

The reaction of the *p*-toluidine with the bridged iodo-complex (PPr$^n_3$)$_2$Pd$_2$I$_4$ indicated that the components are in labile equilibrium in solution:

$$(PPr^n_3)_2Pd_2I_4 + 2C_7H_7NH_2 \rightleftharpoons 2[PPr^n_3,C_7H_7NH_2PdI_2].$$

The mixed product was obtained only by using an excess of amine in the reaction, and by recrystallising the product from a solution of the amine in the appropriate organic solvent (light petroleum, b. p. 60—80°).

The complex [PPh$_3$,C$_7$H$_7$NH$_2$PdCl$_2$] is peculiar in crystallising from alcohols with one molecule of the alcohol tenaciously held in the crystal.

We checked the configuration of the mixed complexes by measuring their $\Delta\varepsilon/f$ in benzene solution ($\Delta\varepsilon$ = the increment in dielectric constant due to the solute, f = mol. fraction of solute), and all had *trans*-configurations, as expected.[5]

Generally it appears that the mixed complexes [L,amPdCl$_2$] have a somewhat similar pattern of relative stabilities to that of their platinous analogues. However, they are less stable and more soluble in organic solvents, and so fewer types can be isolated at ordinary temperatures.

Experimental

Microanalyses are by Messrs. W. Brown and A. G. Olney of these laboratories.

The bridged complexes [L$_2$Pd$_2$Cl$_4$] were prepared as previously described.[3] The low yields of the mixed complexes [L,amPdCl$_2$] reported below are to be attributed to the small scale on which the compounds were prepared and to their high solubilities in organic solvents. The reactions of formation appear to be almost quantitative.

trans-*Triethylphosphinepiperidinedichloropalladium*.—The bridged complex [(PEt$_3$)$_2$Pd$_2$Cl$_4$] (1 g.) in methylene chloride (50 c.c.) was treated with piperidine (0·3 c.c.), and the orange-yellow solution taken to dryness at 15 mm. The residual *product* recrystallised from light petroleum (b. p. 60—80°) (yield 43%) (Found: C, 34·9; H, 6·8; N, 3·9. C$_{11}$H$_{26}$NCl$_2$PPd requires C, 34·7; H, 6·9; N, 3·7%). $\Delta\varepsilon/f$ = 4·3.

Similarly prepared and purified were: trans-*tri*-n-*propylphosphinepiperidinedichloropalladium* (yield 92%) (Found: C, 39·7; H, 7·7; N, 3·75. C$_{14}$H$_{32}$NCl$_2$PPd requires C, 39·75; H, 7·6; N, 3·3%), trans-*triethylarsinepiperidinedichloropalladium* (58%) (Found: C, 31·3; H, 6·3; N, 3·3. C$_{11}$H$_{26}$NCl$_2$AsPd requires C, 31·1; H, 6·2; N, 3·3%), trans-*tri*-n-*propylphosphine*-p-*toluidinedichloropalladium* (37%) (Found: C, 43·3; H, 6·8. C$_{16}$H$_{30}$NCl$_2$PPd requires C,

[5] Cf. Chatt and Wilkins, *J.*, 1953, 70.

43·2; H, 6·8%), and trans-*di*-n-*butylphenylphosphine*-p-*toluidinedichloropalladium* (recrystallised from methanol; yield 20%) (Found: C, 49·7; H, 6·3; N, 2·95. $C_{21}H_{32}NCl_2PPd$ requires C, 49·8; H, 6·4; N, 2·8%).

trans-*Di*-n-*butylphenylphosphinepiperidinedichloropalladium*.—The complex $[(PBu^n_2Ph)_2Pd_2Cl_4]$ (3 g.) was suspended in methanol (25 c.c.), and freshly distilled piperidine (0·7 c.c.) was added. The resultant orange solution on evaporation at 15 mm. left an orange oil. This was induced to crystallise by seeding with the corresponding crystalline *p*-toluidine complex, and the product was purified by making a saturated solution in methanol at room temperature and collecting the *product* which crystallised at −5° (yield 75%) (Found: C, 47·0; H, 7·2; N, 2·75. $C_{19}H_{34}NCl_2PPd$ requires C, 47·1; H, 7·2; N, 2·9%). This compound tends to form oils which are difficult to crystallise.

trans-*Triphenylphosphinepiperidinedichloropalladium* was prepared by shaking a suspension of the stoicheiometric amount of $[(PPh_3)_2Pd_2Cl_4]$ with piperidine in methylene chloride until complete dissolution had occurred. It recrystallised from light petroleum (b. p. 80—100°) (yield 36%) (Found: C, 52·5; H, 5·1; N, 2·95%; *M*, ebullioscopic in 0·8% benzene solution, 543. $C_{23}H_{26}NCl_2PPd$ requires C, 52·6; H, 5·0; N, 2·7%; *M*, 525). It is a non-electrolyte in nitrobenzene solution.

trans-(*Trimethyl Phosphite*)*piperidinedichloropalladium*.—The amine was added to a solution of the bridged compound in methylene chloride at −70°, and the *product* which separated spontaneously was recrystallised from light petroleum (b. p. 60—80°) (yield 25%) (Found: C, 25·1; H, 5·2; N, 3·7. $C_8H_{29}O_3NCl_2PPd$ requires C, 24·8; H, 5·2; N, 3·6%).

Similarly prepared were: trans-(*triphenyl phosphite*)*piperidinedichloropalladium* (33%) (Found: C, 48·1; H, 4·5; N, 2·5. $C_{23}H_{26}O_3NCl_2PPd$ requires C, 48·2; H, 4·6; N, 2·4%); trans-(*trimethyl phosphite*)-p-*toluidinedichloropalladium* (recrystallised from methanol; yield 59%) (Found: C, 29·5; H, 4·4; N, 3·6%; *M*, ebullioscopic in 1·2% benzene solution, 434. $C_{10}H_{18}O_3NCl_2PPd$ requires C, 29·4; H, 4·4; N, 3·4%; *M*, 489), $\Delta\varepsilon/f = 7·6$; and trans-(*triphenyl phosphite*)-p-*toluidinedichloropalladium* (purified, with great loss, by repeated recrystallisation from *cyclo*hexane and then ether–light petroleum) (Found: C, 50·5; H, 4·1%; *M*, ebullioscopic in 0·8% benzene solution, 515. $C_{25}H_{24}O_3NCl_2PPd$ requires C, 50·5; H, 4·1%; *M*, 595), $\Delta\varepsilon/f = 7·9$. The above phosphite complexes are non-electrolytes in nitrobenzene solution.

trans-*Triphenylphosphine*-p-*toluidinedichloropalladium*.—The complex $[(PPh_3)_2Pd_2Cl_4]$ (2 g.) in methylene chloride (50 c.c.) suspension was shaken with *p*-toluidine (0·45 g.) for several hours. The solution was filtered from a small amount of unchanged material and taken to dryness at 15 mm., leaving an orange crystalline residue (2 g.). This product could be satisfactorily recrystallised, as *solvates*, only from methanol (Found: C, 53·6; H, 4·9; N, 2·75. $C_{25}H_{24}NCl_2PPd,CH_4O$ requires C, 53·9; H, 4·9; N, 2·4%), ethanol (Found: C, 54·7; H, 5·3; N, 2·4. $C_{25}H_{24}NCl_2PPd,C_2H_6O$ requires C, 54·7; H, 5·1; N, 2·4%), or propanol (Found: C, 55·2; H, 5·35; N, 2·7. $C_{25}H_{24}NCl_2PPd,C_3H_8O$ requires C, 55·4; H, 5·3; N, 2·3%). Drying the above compounds in a high vacuum caused only partial loss of the alcohol and, when heat was applied, decomposition set in. The products with alcohol of crystallisation are non-electrolytes in nitrobenzene solution.

trans-*Tri*-n-*propylphosphine*-p-*toluidinedi-iodopalladium*.—*p*-Toluidine (0·5 g.) was added to a solution of the complex $[(PPr^n_3)_2Pd_2I_4]$ (2·3 g.) in acetone. No change in colour was observed. The solution was taken to dryness at 15 mm., and on attempted recrystallisation the residue from light petroleum (b. p. 80—100°) re-formed a large amount of the original binuclear complex. *p*-Toluidine was then added in sufficient quantity to redissolve the binuclear complex in the boiling solvent, and then, on cooling, a crop of red plate-like crystals was obtained. Recrystallisation from light petroleum in presence of an excess of *p*-toluidine was repeated. The *product* was then washed with light petroleum (b. p. 40—60°) and dried in a vacuum-desiccator. The yield was poor (Found: C, 30·8; H, 4·7; N, 2·4. $C_{16}H_{30}NI_2PPd$ requires C, 30·6; H, 4·8; N, 2·2%).

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478. *Studies of* Aspergillus niger. *Part VI.* The Separation and Structures of Oligosaccharides from Nigeran.*

By S. A. Barker, E. J. Bourne, D. M. O'Mant, and M. Stacey.

The isolation and characterisation of nigerose (3-*O*-α-D-glucopyranosyl-D-glucose) and the two isomeric trisaccharides [*O*-α-D-glucopyranosyl-(1 ⟶ 3)-*O*-α-D-glucopyranosyl-(1 ⟶ 4)-D-glucose and *O*-α-D-glucopyranosyl-(1 ⟶ 4)-*O*-α-D-glucopyranosyl-(1 ⟶ 3)-D-glucose] obtained from nigeran are described.

It has been shown [1,2] that the intracellular polysaccharide, nigeran, produced by *Aspergillus niger* "152," is an essentially unbranched polyglucosan in which most, if not all, of the residues are attached alternately by α-1 : 4- and α-1 : 3-linkages. We now present additional evidence for the fine structure of nigeran obtained by the separation and structural investigation of the isomeric trisaccharides derived by acidic hydrolysis. A structural investigation of the methyl furanosides of nigerose (3-*O*-α-D-glucopyranosyl-D-glucose) is also reported.

After the isolation of fractions containing mixed disaccharides and mixed trisaccharides,[1,2] the initial problem was to devise a method of separation of the isomers. Attempts to separate maltose and nigerose on Amberlite IRA-400 with a borate buffer, as used by Khym and Zill [3] for other sugar isomers, was unsuccessful owing to the alkali-lability of nigerose (cf. Corbett, Kenner, and Richards [4]). It has been shown [1,2] that the trisaccharide fraction contained two trisaccharides, one of which [T_2, presumed to be *O*-α-D-glucopyranosyl-(1 ⟶ 4)-*O*-α-D-glucopyranosyl-(1 ⟶ 3)-D-glucose] moved at about twice the speed of the other [T_1, presumed to be *O*-α-D-glucopyranosyl-(1 ⟶ 3)-*O*-α-D-glucopyranosyl-(1 ⟶ 4)-D-glucose] on paper ionophoresis [5] in borate buffer (pH 10). Separation of bands of the trisaccharides was effected on paper in this way but elution of the strips with water and subsequent removal of the sodium and borate ions yielded degradation products, particularly in the case of T_2. Since it was shown that the procedure for removing sodium borate (cation-exchange resin and removal of boric acid by codistillation with methanol) did not cause this degradation, it was concluded that the trisaccharides were stable in borate buffer of pH 10·0 while on the paper but not in solution. Undegraded trisaccharides were however obtained by extracting the ionophoresis paper with the calculated quantity of dilute hydrochloric acid so that the resultant pH was *ca.* 5.

To obtain the larger amounts required for structural investigation a method was devised [6] which depended on the fact that one of each pair of isomers was readily converted into its methyl furanosides by treatment with methanolic hydrogen chloride at room temperature and that these furanosides were absorbed more strongly on a charcoal column than was the unchanged sugar Thus a mixture of maltose and nigerose gave chromatographically pure maltose and two fractions [(I), eluted with 10% ethanol; and (II), eluted with 30% ethanol] containing the furanosides of nigerose. These fractions had the same R_P values on a paper chromatogram and the same methoxyl contents and were non-reducing to the Shaffer–Hartmann reagent.[7] Both gave nigerose when hydrolysed with 0·01N-hydrochloric acid at 45°. When either fraction was oxidised with sodium periodate the results were in good agreement with the theoretical values for a methyl furanoside of

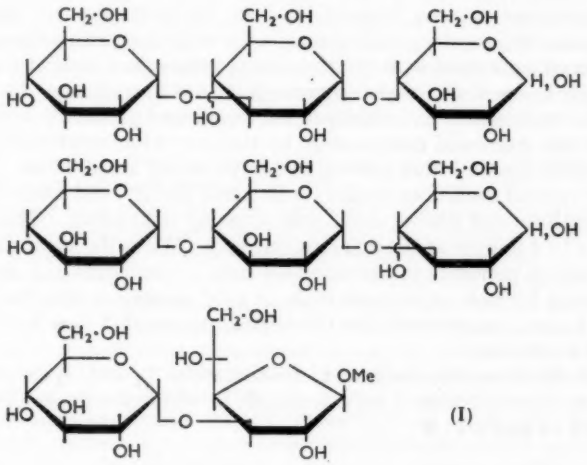
* Part V, *J.*, 1957, 2064.

[1] Barker, Bourne, and Stacey, *J.*, 1953, 3084.
[2] *Idem, Chem. and Ind.*, 1952, 756.
[3] Khym and Zill, *J. Amer. Chem. Soc.*, 1952, **74**, 2090; 1953, **75**, 1339.
[4] Corbett, Kenner, and Richards, *Chem. and Ind.*, 1953, 154.
[5] Foster, *J.*, 1953, 982.
[6] Barker, Bourne, and O'Mant, *Chem. and Ind.*, 1955, 425.
[7] Shaffer and Hartmann, *J. Biol. Chem.*, 1921, **45**, 365.

3-*O*-α-D-glucopyranosyl-D-glucose (3 mols. uptake, 1 mol. of formic acid, 1 mol. of formaldehyde). When the product of periodate oxidation of fraction (I) was reduced with sodium borohydride, hydrolysed with acid, de-ionised, and fractionated on a cellulose column, D-xylose (characterised as its crystalline β-tetra-acetate) was obtained.

Since xylose can only be formed from glucose directly by the removal of $C_{(6)}$, positions 5 and 6 must have been unblocked during the periodate oxidation, and hence the glucoside residue must have been in the furanose form and have been blocked at either position 2 or position 3. The presence of a pair of free hydroxyl groups on $C_{(5)}$ and $C_{(6)}$ having free rotation was also confirmed by the rapidity with which these were oxidised by lead tetra-acetate compared with the remaining pairs of *trans*-hydroxyl groups (cf. Hockett and McClenahan [8]).

Additional evidence for the structure of the materials (I) and (II) was obtained by methylation, hydrolysis, and fractionation of the products on a silica-gel column.[9] A chromatogram of each of the two fractions obtained showed that one was 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose and that the other was a tri-*O*-methyl-D-glucose with an R_F value different from that of 2 : 3 : 5-, 2 : 3 : 6-, or 2 : 3 : 4-tri-*O*-methyl-D-glucose.



The tri-*O*-methyl-D-glucose was shown to have $C_{(4)}$ unblocked because of its ability to undergo methyl-furanoside formation in methanolic hydrogen chloride at room temperature. When the tri-*O*-methyl-D-glucose was reduced to the corresponding sorbitol derivative, the product consumed practically 1 mol. of periodate but produced no formaldehyde and a negligible amount of formic acid. The only two tri-*O*-methylsorbitol derivatives which would be expected to behave in this way and have $C_{(1)}$ and $C_{(4)}$ free were the 2 : 3 : 6- and the 2 : 5 : 6-derivative. Since however the tri-*O*-methyl sugar was distinguishable from the 2 : 3 : 6-derivative chromatographically, it must have been 2 : 5 : 6-tri-*O*-methyl-D-glucose. Ample evidence is therefore available to show that fractions (I) and (II) are predominantly the β- ($[\alpha]_D + 40°$) and the α-methyl furanoside ($[\alpha]_D +128°$), respectively, of 3-*O*-α-D-glucopyranosyl-D-glucose.

Separation of the trisaccharide isomers, T_1 and T_2, effected by preferential furanoside formation and fractionation on a charcoal column, gave chromatographically pure T_1 together with fractions containing the methyl furanosides of T_2 contaminated with varying amounts (7·3—28%) of T_1. The furanosides were easily freed from the T_1 by fractionation

[8] Hockett and McClenahan, *J. Amer. Chem. Soc.*, 1939, **61**, 1667.
[9] Bell, *J.*, 1944, 473.

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on a cellulose column, which appears to be more efficient than a charcoal column for separating a free sugar and the furanosides of an isomeric sugar, although its capacity is more limited.

Trisaccharide T_1 was reducing and contained maltose and nigerose moieties since these disaccharides were isolated after partial acidic hydrolysis and characterised as their β-octa-acetate and osazone respectively. The sequence of linkages was determined by reduction of T_1 to the sugar alcohol and partial acidic hydrolysis of the product. Paper-chromatographic analysis showed that the only reducing disaccharide present was nigerose. This proved that T_1 was mainly *O*-α-D-glucopyranosyl-(1 → 3)-*O*-α-D-glucopyranosyl-(1 → 4)-D-glucose. In close agreement with theoretical predictions (5 mols. of periodate consumed; 2 mols. of formic acid and 2 mols. of formaldehyde produced) the alcohol of T_1 consumed 4·9 mols. of periodate and produced 2·2 mols. of formic acid and 1·9 mols. of formaldehyde. (It will also be recalled that no di-*O*-methyl glucose was detected [1] in the hydrolysate of methylated nigeran.) This evidence excludes the presence of significant quantities of a branched trisaccharide in the T_1 fraction.

The methyl furanosides of T_2 on hydrolysis with 0·01N-hydrochloric acid at 50° gave the reducing trisaccharide T_2 and on further hydrolysis (0·3N-sulphuric acid at 85—90°) produced the disaccharides maltose (characterised as its β-octa-acetate) and nigerose (characterised as its osazone), together with glucose. On oxidation with sodium periodate the results were in good agreement with the theoretical values for a methyl furanoside of *O*-α-D-glucopyranosyl-(1 → 4)-*O*-α-D-glucopyranosyl-(1 → 3)-D-glucose (4 mols. of periodate consumed, 1 mol. each of formaldehyde and formic acid produced). Again 1 mol. of lead tetra-acetate was consumed more rapidly by the pair of hydroxyls on $C_{(5)}$ and $C_{(6)}$ of the furanoside residue than by other pairs of hydroxyls which are all *trans*. Reduction of T_2, effected under neutral conditions because of its alkali lability, and partial hydrolysis of the alcohol gave maltose and glucose as the only reducing saccharides. This confirmed the presence of the α-1 : 4-linkage at the non-reducing end. When the sugar alcohol of T_2 was oxidised with sodium periodate it consumed 6·1 mols. of periodate and produced 2·2 mols. of formic acid and 1·9 mols. of formaldehyde, in good agreement with the theoretical values of 6, 2, and 2 mols., respectively, for *O*-α-D-glucopyranosyl-(1 → 4)-*O*-α-D-glucopyranosyl-(1 → 3)-D-glucitol.

It is evident that the structures assigned to trisaccharides T_1 and T_2 are in complete agreement with those expected from a polysaccharide in which the glucose residues are alternately linked α-1 : 3 and α-1 : 4.

Experimental

Partial Acidic Hydrolysis of Nigeran.—The polysaccharide (97 g.) was hydrolysed in a solution containing water (3·5 l.) and concentrated sulphuric acid (100 c.c.) at 85° for 3·1 hr. The reducing power of the hydrolysate then corresponded to a 47% conversion into glucose. The solution was neutralised with barium carbonate, clarified on a centrifuge, and evaporated *in vacuo* to *ca.* 200 c.c. The saccharide mixture was then fractionated on a charcoal column (*l*, 71 cm.; *d*, 5·5 cm.) by Whistler and Durso's method [10] using increasing concentrations of aqueous ethanol. Elution with water (6·7 l.) removed the glucose while a disaccharide mixture (18·1 g.), containing nigerose and maltose, was eluted with 7% aqueous ethanol (6·8 l.) and 10% aqueous ethanol (2·5 l.). Thereafter elution with 15% aqueous ethanol (20·5 l.) gave fractions containing trisaccharides (9·9 g.), tetrasaccharides (5·8 g.), and higher saccharides (8·8 g.).

Separation of the Disaccharide Fraction by Furanoside Formation.—The disaccharides (4 g.) were treated with 4% methanolic hydrogen chloride (180 c.c.) at room temperature for 74 min. During this time the solution showed $[\alpha]_D^{17}$ +130° (4 min.) → +103° (40 min.) → +101° (73 min.). The solution was neutralised with silver carbonate, the suspension centrifuged, and the methanol removed *in vacuo* over freshly washed barium carbonate below 35°. The syrup

[10] Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677.

was extracted with water (50 c.c.) and fractionated on a charcoal column (17 cm. × 9 cm.²). The charcoal had been previously washed with distilled water until the pH of the washings was the same as that of the distilled water, and then dialysed against running tap-water for 2 weeks. After the column had been washed with water (700 c.c.), 5% ethanol (1·4 l.) eluted the maltose (1·783 g.) while the methyl furanosides of nigerose were obtained (I) with 10% ethanol {1·1 l.; 0·576 g. having $[\alpha]_D^{17}$ +40° (*c* 0·48 in H_2O)} and (II) with 30% ethanol {800 c.c.; 0·703 g. having $[\alpha]_D^{17}$ +128° (*c* 0·49 in H_2O)}.

Examination of the Methyl Furanosides of Nigerose.—Both fractions (I) and (II) were non-reducing to the Shaffer–Hartmann reagent [7] and had OMe 8·2% (a methyl furanoside of nigerose requires OMe, 8·7%).

(i) *Lead tetra-acetate oxidation.* Fraction (II) (26·5 mg.) was dissolved in dry glacial acetic acid (25 c.c.), and a saturated, standardised solution of lead tetra-acetate in dry glacial acetic acid (4 c.c.) added. The solution was diluted to 50 c.c. with glacial acetic acid and kept at 25° in a flask which was wrapped in aluminium foil to exclude light. The uptake of lead tetra-acetate (moles per mole of furanoside) was 0·7 hr., 0·07; 1·7 hr., 0·15; 4·7 hr., 0·35; 10·5 hr., 0·57; 23·5 hr., 0·83; 47·5 hr., 1·06; 101 hr., 1·34; 192 hr., 1·63.

(ii) *Periodate oxidation.* Fraction (II) (53·3 mg.) was treated with 0·075M-sodium periodate (50 c.c.) in the dark at room temperature. The number of moles of sodium periodate consumed per mole of furanoside was: 5 min., 1·5; 15 min., 2·3; 60 min., 2·4; 120 min., 2·7; 1140 min., 3·1. After 1140 min., 1·0 mole of formic acid and 1·2 moles of formaldehyde (isolated as methylene-bisdimedone, m. p. and mixed m. p. 192°) were produced per mole of furanoside.

Fraction (I) when treated as above consumed 1·9 moles (5 min.), 2·5 moles (60 min.), 2·6 moles (120 min.), 3·0 moles (1110 min.) of periodate per mole of furanoside. After 1110 min., 1·1 moles of formic acid and 0·8 mole of formaldehyde (characterised as above) were produced per mole of furanoside.

(iii) *Conversion of the product of periodate oxidation into xylose.* Fraction (I) (259 mg.) was treated in the dark with sodium periodate (350 mg.) in water (100 c.c.), at room temperature for 36 hr. Excess of periodate was then destroyed by the addition of ethylene glycol (0·5 ml.), and the solution concentrated *in vacuo* below 30° to 25 c.c. Sodium borohydride (250 mg.) was added and the solution kept overnight at room temperature. Excess of borohydride was then destroyed by the addition of Amberlite IR-120. The resin was filtered off and the solution was made N with respect to sulphuric acid. After 2 hr. at 100° the solution was cooled and free iodine extracted from it with carbon tetrachloride. After neutralisation with barium carbonate the solution was clarified in the centrifuge and evaporated *in vacuo* to a syrup which was distilled three times with dry methanol in order to remove the methyl borate. This syrup was fractionated on a cellulose column (23 cm. × 8 cm.²) which was developed with butanol–ethanol–water–ammonia (40 : 16 : 20 : 1). Those fractions which only contained a component with the same R_F value as xylose were combined and concentrated to a syrup (33 mg.) having $[\alpha]_D$ +15° in water. On acetylation of the syrup with sodium acetate and acetic anhydride, crystals (7 mg.) were obtained having m. p. 124—125°, not depressed on admixture with β-tetra-*O*-acetyl-D-xylose.

(iv) *Methylation of the furanosides of nigerose.* A mixture of fractions (I) and (II) (550 mg.) was methylated in dioxan (25 c.c.) at 40° by alternate additions of dimethyl sulphate (20 c.c.) and 30% aqueous sodium hydroxide (40 c.c.) in ten equal amounts. After the resulting mixture had been stirred for 3 days at room temperature, water (50 c.c.) was added and the mixture heated at 90—95° for 30 min. The methylated product was extracted with chloroform (10 × 25 c.c.), and the syrup (442 mg.) obtained by concentrating the dried extract then submitted to three further methylations with Purdie reagents. A portion (2 mg.) of the product (0·362 g.) was hydrolysed and the products were separated on a paper chromatogram irrigated with the organic phase of butanol–ethanol–water–ammonia (40 : 10 : 49 : 1). Only two spots could be detected; they had R_F values (i) identical with that of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose and (ii) somewhat less than that of 2 : 3 : 6-tri-*O*-methyl-D-glucose.

(v) *Separation and examination of the products from the hydrolysis of the methylated nigerose furanosides.* The methylated product (325 mg.) was refluxed with 4% methanolic hydrogen chloride (30 c.c.) for 4 hr. The solution was neutralised with silver carbonate, clarified in the centrifuge, and evaporated *in vacuo* to a syrup. These glycosides were then hydrolysed with 0·5N-HCl for 4 hr. at 100°. After the solution had been freed from ions as above the resulting methyl sugars (191 mg.) were fractionated on a silica column by Bell's method.[9]

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Elution with chloroform gave a fraction (120 mg.) which behaved in a manner identical with that of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose when examined on a paper chromatogram irrigated as above. A second fraction (38 mg.) contained the unknown tri-*O*-methyl sugar which had an R_P value (0·62) different from that of 2 : 3 : 5-tri-*O*-methyl- (R_P 0·67), 2 : 3 : 6-tri-*O*-methyl- (R_P 0·66), and 2 : 3 : 4-tri-*O*-methyl-D-glucose (R_P 0·68). It had $[\alpha]_D$ +48° (*c* 0·68 in $CHCl_3$).

(vi) *Examination of the unknown tri-O-methyl sugar.* The tri-*O*-methyl-D-glucose fraction (34 mg.) was treated with 4% methanolic hydrogen chloride (6 c.c.) at room temperature. The solution had $[\alpha]_D^{17}$ +53° (4 min.) ⟶ +39° (32 min.) ⟶ +35° (67 min.). The tri-*O*-methyl sugar was regenerated by concentration to a syrup, hydrolysis with 0·1N-hydrochloric acid (10 c.c.) at 100° for 3 hr., and subsequent neutralisation with silver carbonate and concentration of the filtered solution *in vacuo*.

The tri-*O*-methyl sugar was dissolved in water (5 c.c.) and treated with aqueous sodium borohydride (60 mg. in 5 c.c.) at room temperature for 18 hr. After removal of ions as described above, the solution was concentrated to a non-reducing syrup (13·2 mg.). When submitted to periodate oxidation under the conditions described for fraction (I), the tri-*O*-methylhexitol consumed 0·3 mole (2·3 hr.), 0·7 mole (14·1 hr.), 0·9 mole (22·1 hr.), 0·9 mole (27·1 hr.) of periodate per mole of tri-*O*-methyl hexitol. After 27·1 hr., it produced 0·1 mole of formic acid per mole of tri-*O*-methylhexitol, but no formaldehyde.

(vii) *Partial acidic hydrolysis of the nigerose furanosides.* Fraction (I) (172 mg.) was treated with 0·01N-hydrochloric acid (172 c.c.) at 45—55°. The reducing power (expressed as mg. of glucose/2 c.c. of solution) of the solution was determined at intervals (see Table) by using the Shaffer–Hartmann reagent.[7]

Time (hr.)	5	10	27	32	37	50	57
Reducing power	0·26	0·44	0·60	0·63	0·64	0·65	0·65

At the same intervals, aliquot parts (2 c.c.) were withdrawn and analysed by paper ionophoresis in borate buffer.[5] This revealed the progressive formation of nigerose; no other reducing sugar was detected.

After 57 hr., the solution was neutralised with silver carbonate, clarified in the centrifuge, evaporated *in vacuo* to a small volume, and freeze-dried (120 mg.). The recovered nigerose showed $[\alpha]_D$ +137° (*c* 0·17 in H_2O).

The above experiment was repeated on fraction (II) on a smaller scale and gave similar results.

Separation of the Trisaccharide Fraction by Furanoside Formation.—The trisaccharide fraction contained two components which could be separated by ionophoresis [5] in borate buffer of pH 10. The slower-moving trisaccharide was designated T_1, and the faster-moving trisaccharide was designated T_2.

A trisaccharide mixture (6·701 g.) was treated with 4% methanolic hydrogen chloride (150 c.c.) at room temperature for 81 min. During this time the solution had $[\alpha]_D^{17}$ +161° (8 min.) ⟶ +141° (40 min.) ⟶ +139° (80 min.). The solution was neutralised with silver carbonate (30 g.), clarified in the centrifuge, and evaporated *in vacuo* at 30° over freshly washed barium carbonate, and the residue taken up in water and filtered. The solution was then passed down a charcoal column (16 cm. × 14 cm.^{2}). Elution with 13% ethanol (6 l.) gave chromatographically pure trisaccharide T_1 (1·646 g.) and later mixed fractions (0·879 g., 0·261 g., 0·640 g., 0·505 g.) in which the presumed furanosides of T_2 were accompanied by progressively decreasing concentrations (28, 8·3, 7·5, 7·3%) of T_1 when estimated by the Shaffer–Hartmann method [7] for reducing power. The major portion of these fractions was refractionated on cellulose columns with butanol–ethanol–water–ammonia (40 : 16 : 20 : 1). Distinct separations were achieved between the furanosides of T_2 and trisaccharide T_1, and these were recovered in yields of 1·452 g. and 0·210 g. respectively.

Examination of Trisaccharide T_1.—The trisaccharide was reducing, and 3 mg. of T_1 exhibited the same reducing power as 0·77 mg. of glucose (Shaffer–Hartmann method [7]). It had $[\alpha]_D$ +169·5° (*c* 1·25 in H_2O). Its infrared spectrum showed strong absorption at 917, 841, and 835 cm.$^{-1}$ (the last two are indicative of α-linkages) and moderate absorption at 796 and 774 cm.$^{-1}$. Hydrolysis of the trisaccharide (8·07 mg.) with 1·5N-sulphuric acid at 100° for 5 hr. gave glucose (identified on a paper chromatogram) in an amount corresponding to a 97·5% conversion.

(i) *Partial acidic hydrolysis.* The trisaccharide T_1 (1 g.) was submitted to partial acidic

hydrolysis with 0·3N-sulphuric acid (20 c.c.) at 85—90° for 45 min. After neutralisation with barium carbonate the solution was passed down a charcoal column. The glucose was removed by water-washing, and the mixture of disaccharides (0·093 g.) eluted with 8% aqueous ethanol. The nigerose and maltose mixture was separated by furanoside formation and then fractionated on a cellulose column as previously described. This yielded maltose (35 mg.) and the furanosides of nigerose (43 mg.). The maltose was characterised by conversion into its β-octa-acetate (12 mg.), m. p. and mixed m. p. 159—160°. The furanoside of nigerose was hydrolysed to nigerose (as above), and this was characterised by conversion into the osazone (23 mg.), m. p. and mixed m. p. 204—206°.

(ii) *Reduction to the sugar alcohol.* Trisaccharide T_1 (100 mg.) was treated with aqueous sodium borohydride (100 mg. in 50 c.c.) at room temperature for 3 hr. After removal of ions as described above, the trisaccharide alcohol (65 mg.) was recovered by freeze-drying.

Some (10 mg.) of the alcohol was partially hydrolysed with 0·3N-sulphuric acid (1 c.c.) at 90° for 45 min. After neutralisation with barium carbonate and filtration, paper chromatography (for reducing sugars) revealed glucose, nigerose, and a trace of T_1. No maltose could be detected.

The remainder (51·8 mg.) of the sugar alcohol of T_1 was oxidised with sodium periodate as described above. The number of moles of periodate consumed per mole of trisaccharide alcohol was 2·4 (0·25 hr.), 2·5 (0·5 hr.), 3·0 (1 hr.), 3·9 (4 hr.), 4·7 (18 hr.), 4·9 (23 hr.), 4·9 (28 hr.). The corresponding figures, after 28 hr., for formic acid and formaldehyde produced were 2·2 moles and 1·9 moles, respectively.

The solution from the oxidation was made N with respect to sulphuric acid and heated at 100° for 3 hr. Free iodine was extracted with carbon tetrachloride, and sodium ions were removed from the solution with Amberlite IR-120. The solution was then neutralised with barium carbonate, and clarified by centrifuging. Analysis on a paper chromatogram revealed glucose.

Examination of the Methyl Furanosides of Trisaccharide T_2.—The presumed furanosides were non-reducing to the Shaffer–Hartmann reagent [7] and had OMe 6·1% (a methyl furanoside of a trisaccharide requires OMe, 6·0%).

(i) *Periodate oxidation.* The furanosides (96·3 mg.) were oxidised with sodium periodate as described above. The number of mols. of periodate consumed per mol. of furanosides was 3·0 (0·25 hr.), 3·2 (0·5 hr.), 3·4 (1 hr.), 3·7 (4 hr.), 3·9 (18 hr.), and 3·9 (27 hr.). After 27 hr., 0·7 mole of formaldehyde and 1·2 moles of formic acid were produced per mole of furanoside.

(ii) *Lead tetra-acetate oxidation.* The furanosides of T_2 (24·9 mg.) were oxidised with lead tetra-acetate as described for the oxidation of the furanosides of nigerose:

Time (hr.)	1	15	22	88	136	232	287	321
Uptake of $Pb(OAc)_4$ (mols.)	0·12	1·03	1·20	2·13	2·61	3·28	3·51	3·59

(iii) *Conversion into trisaccharide T_2.* The furanosides (370 mg.) were heated in 0·01N-sulphuric acid at 50° for 5 days. Ionophoresis in borate buffer (pH 10·0) showed the presence of trisaccharide T_2 only and this was recovered by neutralising the solution with barium carbonate, then centrifuging and freeze-drying it to a powder (0·308 g.).

(iv) *Conversion into maltose and nigerose.* The furanosides of T_2 (900 mg.) were submitted to partial acidic hydrolysis, and the products separated as described for trisaccharide T_1. A mixture (87 mg.) of maltose and nigerose was obtained from which maltose (37 mg.) and the furanosides of nigerose (39 mg.) were isolated. The maltose was characterised as its β-octa-*O*-acetate (16 mg.), m. p. and mixed m. p. 159—160°. The furanosides of nigerose were hydrolysed to nigerose and this was characterised by conversion into the osazone (28 mg.), m. p. and mixed m. p. 203—206°.

Examination of Trisaccharide T_2.—Its infrared spectrum showed strong absorption at 917, 843, and 835 cm.$^{-1}$ (the last two are indicative of α-linkages) and moderate absorption at 797 and 770 cm.$^{-1}$. Hydrolysis of the trisaccharide (10·4 mg.) with 1·5N-sulphuric acid at 100° for 5 hr. gave glucose (identified on a paper chromatogram) in an amount corresponding to a 99·7% conversion.

(i) *Reduction to the sugar alcohol.* The trisaccharide T_2 (150 mg.) was dissolved in water (40 c.c.), and Raney nickel (0·5 g. in ethanol) was added. The mixture was heated and stirred in an autoclave at 140° with an initial hydrogen pressure of 100 atm. which rose to 135 atm. during the heating time (3 hr.). After cooling, the Raney nickel was filtered off and the solution

freeze-dried (136 mg.). The product was non-reducing to the Shaffer–Hartmann reagent [7] and moved as a single component on a paper chromatogram.

(ii) *Partial hydrolysis of the sugar alcohol.* Part (10 mg.) of the product was submitted to partial hydrolysis with 0·3N-sulphuric acid at 90° for 45 min. Paper chromatography of the neutralised hydrolysate showed that the only reducing sugars present were glucose and maltose.

(iii) *Periodate oxidation of the sugar alcohol.* The remainder (119·5 mg.) of the sugar alcohol was oxidised with sodium periodate as previously described. The consumption of periodate (moles per mole of trisaccharide alcohol) was 3·9 (1 hr.), 5·4 (7 hr.), 6·1 (21 hr.), 6·1 (24·5 hr.). After 24·5 hr., 2·2 mols. of formic acid and 1·9 mols. of formaldehyde were produced.

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479. *The Nucleotide Sequence in Deoxypentosenucleic Acids. Part IV.* The Deoxyribonucleic Acid of* Mycobacterium phlei.

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The deoxyribonucleic acid of *Mycobacterium phlei* has been isolated, characterised, and treated with mercaptoacetic acid at 37° in the presence of zinc chloride and anhydrous sodium sulphate. The resulting *aldehydo*-apurinic acid di(carboxymethyl) dithioacetal was degraded at pH 12 at 37° and the components so produced were separated into 20 fractions by paper chromatography and paper electrophoresis. Eight components have been identified and their proportions in the total hydrolysate determined. From these results, and by their comparison with those obtained previously from studies on calf-thymus deoxyribonucleic acid, it appears that either the chemical degradation proceeds differently in the two nucleic acids, or the nucleotides in one or both of the nucleic acids are not distributed randomly.

PREVIOUS papers [1] have reported a chemical method for the specific degradation of calf-thymus deoxyribonucleic acid, in which the nucleic acid was treated with mercaptoacetic acid in the presence of zinc chloride and anhydrous sodium sulphate, and the resulting *aldehydo*apurinic acid di(carboxymethyl) dithioacetal degraded at pH 12 at 37°. This cleaved the phosphodiester linkages, which in the original deoxyribonucleic acid were to purine nucleotides, but left mainly intact the linkages between pyrimidine nucleotides. The results showed that the pyrimidine nucleotides occurred singly, in pairs, and in groups of three, but that a simple uniform arrangement, such as alternate purines and pyrimidines did not occur.

The deoxyribonucleic acid of *Mycobacterium phlei* has now been subjected to the same procedure. Comparison of the results obtained for the two nucleic acids may indicate whether or not, in deoxypentose nucleic acids, the nucleotides are arranged randomly, as has been discussed in the case of pentosenucleic acids by Gamow and Ycas.[2]

The deoxyribonucleic acid was isolated from *Mycobacterium phlei* as previously described, protein being removed by the use of chloral hydrate.[3] Difficulty was experienced in completely removing the ribonucleic acid which contaminated the product. Fractionation by means of the " Cetrimide " salts, or by adsorption on charcoal,[4] which had been successful in previous cases, did not give a satisfactory product. It appeared

* Part III, *J.*, 1956, 2584.

[1] Jones and Letham, *J.*, 1956, 2573; Jones, Letham, and Stacey, *ibid.*, pp. 2579, 2584.
[2] Gamow and Ycas, *Proc. Nat. Acad. Sci. U.S.A.*, 1955, **41**, 1011; Gamow, *Sci. American*, 1955, **192**, No. 4, p. 70.
[3] Jones and Marsh, *Biochim. Biophys. Acta*, 1954, **14**, 559.
[4] Dutta, Jones, and Stacey, *ibid.*, 1953, **10**, 613.

from this and other work that, when the nucleic acids are isolated under mild conditions, the ribonucleic acid remains relatively undegraded and, therefore, resembles closely the deoxyribonucleic acid in physical properties, thus making difficult the separation of the two types of nucleic acid. Final traces of ribonucleic acid were removed by treatment with crystalline ribonuclease (free from deoxyribonuclease) followed by fractionation with "Cetrimide." The deoxyribonucleic acid contained more guanine and cytosine than adenine and thymine. The low recovery of purines and pyrimidines with respect to phosphorus was probably due to the presence of a phosphorus-containing impurity (*e.g.*, a polyphosphate).

The reaction with mercaptoacetic acid was carried out by a slight modification of the previous method.[1] During the reaction, the purines were completely liberated, about 12% of the phosphorus was rendered dialysable, and the resulting dithioacetal contained the theoretical amount of sulphur. The products of the alkaline degradation of this dithioacetal were separated into 20 components by paper chromatography in propan-2-ol–ammonia and by paper electrophoresis at pH 3·5. Owing to the comparatively small amount of deoxyribonucleic acid available, and to the small proportion of some of the components present, sufficient material could not be obtained for complete pyrimidine, phosphorus, and sulphur analyses on all of the components. Some were identified by comparison with similar substances identified in hydrolysates of calf-thymus *aldehydo*-apurinic acid di(carboxymethyl) dithioacetal. For the estimation of cytosine and thymine, a spectrophotometric method was used, which gave results within 10% of those obtained by the usual hydrolysis followed by paper chromatography and could be applied to the identification of the small homogeneous components. The amounts of each component present were estimated by cutting the paper chromatograms and electrophoretograms into strips, eluting these, and measuring the optical density at 276 mμ. This method accounts for about 80% of the ultraviolet-absorbing material of the hydrolysate.

TABLE 1. *Components of the alkaline hydrolysate of the* aldehydo*apurinic acid di(carboxymethyl) dithioacetal of* Mycobacterium phlei *and of calf thymus.*

	% of the total pyrimidines				
	Detd. in dithioacetal from		Calculated ‡ (on basis of random distribution)		
Component †	*Myco. phlei* *	Calf thymus *	Sequence of pyrimidines	*Myco. phlei*	Calf thymus
T	2·0	3·0	t	7·8	13·8
C	4·0	2·0	c	17·3	11·3
T–P–C	3·0	4·5	tc	10·6	12·4
T–P–T	0	2·0	tt	2·5	7·6
C–P–C	1·5	1·5	cc	11·9	5·1
T–P–S–P	0·5	9·0	Trinucleotides + larger oligonucleotides	50·0	50·0
C–P–S–P	2·0	4·5			
T–P–T–P–S–P	?	5·0			
T–P–C–P–S–P	1·0	10·0			
T–P–T–P–C–P–S–P	1·0	3·0			
Zone 1	62·5	45·0			

* To the nearest 0·5%. † T = thymidine residue; C = deoxycytidine residue; S = *aldehydo*-2-deoxy-D-ribose, di(carboxymethyl) dithioacetal residue; P = phosphate residue. The sequence in each component has not been determined. ‡ See text.

Results are in Table 1. The "calculated" figures are derived by the following mathematical treatment, for which we are indebted to Dr. A. R. Peacocke.

Consider a large number of linear arrays each containing $N/2$ purines and $N/2$ pyrimidines, in which each site has an equal chance of being occupied by a purine or a pyrimidine. This latter condition corresponds to the observation that in deoxyribonucleic acid

$$[\text{adenine}] + [\text{guanine}] = [\text{cytosine}] + [\text{thymine}]$$

The number of sequences of n pyrimidines will be $N/2^{n+2}$, *i.e.*, the number of sequences of 1, 2, and 3 pyrimidines will be $N/2^3$, $N/2^4$, and $N/2^5$ respectively.

The total number of pyrimidines occurring in all unbroken sequences of length n will be $Nn/2^{n+2}$. If it is assumed that $N \gg n$ and that there is a very large number of arrays of N units, the total number of pyrimidines in a given array of N will be on the average $N \sum_{0}^{\infty} n/2^{n+2}$, $= \frac{1}{2}N$, as at first assumed.

Hence the fraction of pyrimidines occurring singly $(n = 1) = N/2^3 \div N/2 = \frac{1}{4}$, and the fraction occurring in pairs $(n = 2) = 2N/2^4 \div N/2 = \frac{1}{4}$. Therefore the fraction of pyrimidines occurring in sequences greater than two $(n > 2) = \frac{1}{2}$.

Let the fraction of pyrimidines which are cytosine (c) and thymine (t) be c and t respectively. Then in deoxyribonucleic acid $c + t = 1$. For single units of pyrimidines, the fraction of pyrimidines occurring as cytosine will be $c/4$ and those occurring as thymine will be $t/4$.

For units of two pyrimidines, $c^2/4$ will occur as cc, $2ct/4$ as ct, and $t^2/4$ as tt.

For units containing n nucleotides the proportions of the various arrangements can be obtained by expansion of $(c + t)^n = 1$.

Although many of the components from both *Myco. phlei* and calf-thymus deoxyribonucleic acids have not been identified, certain differences between the two nucleic acids can be seen (Table 1). Thus, the proportion of pyrimidines in zone 1 (which probably contains mainly trinucleotides and larger oligonucleotides) is much higher from *Myco. phlei* deoxyribonucleic acid than from calf-thymus deoxyribonucleic acid. This makes the proportion of the other components correspondingly lower, except that of the mononucleosides which are present in similar amounts in the two cases. The explanation of this result cannot be that cytosine-containing components have lower R_F values than thymine-containing ones, since this is not so with mono- and di-nucleotide derivatives. If it is assumed (*a*) that the pyrimidines in deoxyribonucleic acid are distributed randomly, (*b*) that the non-specific degradation of the deoxyribonucleic acid which may occur on treatment with mercaptoacetic acid is not influenced by the type of pyrimidine nucleotide undergoing fission, and (*c*) that the mode of fission occurring during the alkaline degradation of the *aldehydo*apurinic acid di(carboxymethyl) dithioacetal is also not influenced by the type of nucleotide, then it would be expected that the ratio of the amount of one component obtained from one deoxyribonucleic acid to that of the same component from a second deoxyribonucleic acid would be the same as the ratio of the calculated probabilities of the occurrence of the particular sequence in the two nucleic acids. The results (Table 1) show that this is not the case, the most significant deviations being with the components, T–P–C–P–S–P and C–P–C. In the hydrolysate of the dithioacetal from one deoxyribonucleic acid, if the above conditions held, the proportions of the amounts of the dinucleoside phosphates to each other would be proportional to the probability of the occurrence of the particular sequence. This is approximately so with the dinucleoside phosphates from calf-thymus deoxyribonucleic acid, but not with those from *Myco. phlei* deoxyribonucleic acid, the amount of di(deoxycytidine) phosphate being only half that which would be expected from the amount of thymidine–deoxycytidine phosphate found.

These results indicate that one or more of the conditions outlined above do not apply. With respect to (*b*), the amount of dialysable phosphorus produced during formation of the dithioacetal should give a measure of the non-specific degradation. Calf-thymus deoxyribonucleic acid gave 6% and *Myco. phlei* deoxyribonucleic acid gave 12% of dialysable phosphorus. This difference fails to account for the observed differences in the amount of zone 1. Furthermore, in recent experiments with calf-thymus deoxyribonucleic acid in which 12% of dialysable phosphorus was produced upon conversion into the dithioacetal, again about 45% of zone 1 was obtained. These results suggest that in one or both of these deoxyribonucleic acids, the nucleotides are not randomly distributed, although the possibility must not be overlooked that the type of pyrimidine influences the mode of

breakdown of the nucleic acid. A definite conclusion on this point should be made possible by the complete identification of all the components from both deoxyribonucleic acids.

Experimental

Nitrogen was determined by the method of Ma and Zuazaga,[5] phosphorus by that of Jones, Lee, and Peacocke,[6] and sulphur by that of Jones and Letham.[7] The purine and pyrimidine contents of *Myco. phlei* deoxyribonucleic acid and the corresponding *aldehydo*apurinic acid di(carboxymethyl) dithioacetal were determined by hydrolysis with anhydrous trifluoroacetic acid at 155° for 50 min. This reagent gave a slightly better recovery of thymine than did formic acid. The purines and pyrimidines were separated by paper chromatography in propan-2-ol–hydrochloric acid [8] and estimated spectrophotometrically.

Phosphomonoesterase was prepared from human prostate gland by Markham and Smith's method.[9] Previously (Part III) this enzyme was state to have ribonuclease activity. It has now been shown that this was not the case, the previous results possibly being due to the presence of enzyme in the ribonucleic acid used for the estimation.

Isolation of Mycobacterium phlei *Deoxyribonucleic Acid.—Mycobacterium phlei* Söhn was grown on a medium (5 l.) containing Lab. Lemco 1%, Oxoid bacteriological peptone 1%, sodium chloride 0·5%, and glycerol 5%, distributed in portions (500 ml.) in mould-culture flasks. The cells were harvested after 14 days' growth at 37° and the nucleic acids isolated by Jones and Marsh's method [3] with the use of chloral hydrate to remove most of the protein. The product thus isolated (1·52 g.) contained 20—40% of ribonucleic acid. Attempts to remove this by fractionation of the " Cetrimide " salts or by adsorption on charcoal [4] were not completely successful although both methods substantially reduced the amount of ribonucleic acid present. After treatment by these two methods, the remaining ribonucleic acid was degraded with crystalline pancreatic ribonuclease (free from deoxyribonuclease), the enzyme was removed as a gel by shaking the solution with chloroform and octanol (9 : 1), and the deoxyribonucleic acid in the aqueous phase was purified *via* the " Cetrimide " salt.[4] The material finally isolated had the following composition :

Nitrogen (%)	Phosphorus (%)	Moles of base/4 g.-atoms of phosphorus				
		Guanine	Cytosine	Adenine	Thymine	Total
14·6	8·8	1·31	1·30	0·60	0·59	3·80

No ribonucleic acid could be detected. The recovery of bases relative to phosphorus was lower than the theoretical value. This may have been due to the presence in this nucleic acid of a small amount of a polyphosphate, the presence of which was indicated by the formation of a small, granular, phosphorus-containing precipitate on the addition of barium chloride at pH 7.

Mycobacterium phlei aldehydo*Apurinic Acid Di(carboxymethyl) Dithioacetal.*—Preliminary experiments indicated that the reaction with mercaptoacetic proceeded better with deoxyribonucleic acid which had been dried *in vacuo* over phosphoric anhydride at 110° for 90 min. than with that which had been more extensively dried (100° *in vacuo* over phosphoric anhydride for 12 hr.). In the latter case, only 90% of the theoretical amount of sulphur was incorporated into the product, although there was complete liberation of guanine.

Myco. phlei deoxyribonucleic acid (340 mg. dry wt.), dissolved in 98% mercaptoacetic acid (8·8 ml.), was treated with a solution of anhydrous zinc chloride (1·98 g.) in mercaptoacetic acid (5·5 ml.), containing in suspension anhydrous sodium sulphate (1·06 g.), for 24 hr. at 37°, the whole being shaken at frequent intervals. Ether (8 vols.) was then added, and the resulting precipitate centrifuged off, washed with ether (3 times), and shaken overnight with a solution of glycine (2 g.) in acetate buffer (pH 6·0; 40 ml.). The resulting suspension was dialysed for a total of 6 days against two portions (2 × 1 l.) of 0·5% glycine solution and then centrifuged. The precipitate was extracted with 5% glycine solution and the extract dialysed against 1% glycine solution. The supernatant liquid and the 5% glycine extract were combined and

[5] Ma and Zuazaga, *Ind. Eng. Chem. Anal.*, 1942, **14**, 280.
[6] Jones, Lee, and Peacocke, *J.*, 1951, 623.
[7] Jones and Letham, *Analyst*, 1956, **81**, 15.
[8] Wyatt, *Biochem. J.*, 1951, **48**, 584.
[9] Markham and Smith, *Biochem. J.*, 1952, **52**, 558, 565.

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centrifuged and the supernatant liquid dialysed exhaustively against tap-water and finally against distilled water. Freeze-drying the solution gave the dithioacetal as a white flocculent solid (280 mg.) which contained no purines and 1·30 moles of cytosine, 0·59 mole of thymine, and 3·80 g.-atoms of sulphur per 4 g.-atoms of phosphorus. No free aldehyde groups could be detected.

The ethereal mother-liquors contained about 2% of the cytosine which was originally present in the deoxyribonucleic acid, but no thymine. During the isolation 12% of the total phosphorus diffused through the Cellophane membranes.

Alkaline Degradation of the Dithioacetal.—The dithioacetal (40 mg.) was dissolved in sodium hydroxide (pH 12; 30 ml.) and kept at this pH for 26 hr. at 37° (dilute sodium hydroxide being added at intervals as necessary). The solution was then neutralised with dilute acetic acid and dialysed. The amount of ultraviolet-absorbing material diffusing through the Cellophane membrane was measured by diluting samples with 0·1N-hydrochloric acid and measuring the optical density at 268 mμ (the wavelength at which the molecular extinctions of thymidylic acid and deoxycytidylic acid coincide at pH 1). When the dialysis was conducted against distilled water, 81% of the material diffused through the membrane and the remainder diffused through upon dialysis against M-sodium chloride.

The neutralised alkaline hydrolysate was separated by chromatography on Whatman No. 3 paper in propan-2-ol–water–ammonia (*d* 0·880) (70 : 30 : 6) into 10 zones. The % of the pyrimidines in each zone was determined as described previously [1] and the total equated to 100%. The properties of the various zones were as follows:

Zone	1	2	3	4	5	6	7	8	9	10
R_F	—	—	—	—	—	0·15	0·24	0·42	0·60	0·67
R_C *	0·07	0·15	0·24	0·37	0·69	1·20	1·60	—	—	—
% of total pyrimidine	62·5	8·3	5·2	3·1	5·3	1·8	3·8	4·4	3·8	2·0

* R_C = distance moved by zone/distance moved by cytidylic acid.

The components of the various zones were prepared by elution of a number of chromatograms. They were then run in the same solvent system before and after re-hydrolysis at pH 12. In neither case was there a significant change in R_C value. The components of zones 2, 3, 4, and 8 were then separated by paper electrophoresis at pH 3·5 into a total of 14 fractions the properties of which are shown in Table 2.

Pyrimidine Analyses.—Owing to the small quantities of these fractions available, it was not possible to determine the pyrimidine contents in the usual way. A method was developed, therefore, in which the pyrimidines were determined spectrophotometrically without prior hydrolysis or chromatographic separation. This depended on the fact that, at pH 1, the maximum optical absorption of thymidylic acid is at 267 mμ and that of deoxycytidylic acid is at 280 mμ. Hence, from measurements at these two wavelengths, the proportions of each of these nucleotides present in a mixture of the two could be calculated. When applied to zones of known composition, the method gave results which were within 10% of that expected. The error was probably due to interaction between the bases in the di- and the tri-nucleotide components. Despite this error, however, the method could be used as a semiquantitative measure of the base content of the smaller components and, when taken with other evidence, could be used in their identification. The results are recorded in Table 2.

Identification of the Components.—Zone 10. This zone was not further resolved by any method tried. It contained thymine and 2-deoxy-D-ribose residues, but no cytosine, sulphur, or phosphorus. It was identified as thymidine by comparison with authentic material.

Zone 9. This was similar to Zone 10 but contained cytosine instead of thymine. It was identified as deoxycytidine by comparison with authentic material.

Zone 8. This sulphur-free zone was separated by paper electrophoresis at pH 3·5 into two components, 8A and 8B. The pyrimidine contents of these were estimated by the spectrophotometric method. 8A contained 1·0 mole of thymine and 0·8 mole of cytosine per g.-atom of phosphorus, and 8B contained 2·2 moles of cytosine per g.-atom of phosphorus. Treatment of 8A and 8B with phosphomonoesterase did not alter their R_F values in the propan-2-ol–ammonia solvent. This showed the absence of a terminal phosphate group. The identification as dinucleoside phosphates as indicated in Table 2 was consistent with their electrophoretic behaviour. No dithymidine phosphate was detected, although from previous work with calf-thymus deoxyribonucleic acid,[1] it would be expected to occur in zone 8.

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TABLE 2. *Properties of the components of the alkaline hydrolysate of* Myco. phlei aldehydo*apurinic acid di(carboxymethyl) dithioacetal.*

Zone	% of total pyrimidines	Thymine / Cytosine (moles) †	Proposed structure *	Zone	% of total pyrimidines	Thymine / Cytosine (moles) †	Proposed structure *
1	62·5	0·50	—	4A	0·6	Thymine only	T–P–S–P
2A	1·0	1·9	T–P–T–P–C–S–P				
2B	1·4	1·1	C–P–T–P–S–P	4B	2·1	Cytosine only	C–P–S–P
2C	1·8	0·60	—				
2D	1·9	0·50	—	4C	0·4	1·2	—
2E	1·2	0·60	—	5	5·3	—	—
2F	1·0	—	—	6	1·8	—	—
3A	2·7	1·0	—	7	3·8	—	—
3B	1·6	Cytosine only	—	8A	2·9	1·2	C–P–T
				8B	1·5	Cytosine only	C–P–C
3C	0·8	Thymine only	—				
				9	3·8	Cytosine only	C
				10	2·0	Thymine only	T

* T = Thymidine residue; C = deoxycytidine residue; S = *aldehydo*-2-deoxy-D-ribose di(carboxymethyl) dithioacetal residue; P = phosphate residue. The sequences within zones 2A and 2B have not been determined, these being only possibilities. † Semiquantitative determination.

Zone 4. This zone separated into components 4A, 4B, and 4C, on electrophoresis at pH 3·5. The identification of 4A and 4B, as indicated in Table 2, was made from the base contents and by comparison of their behaviour upon paper chromatography and paper electrophoresis with components already identified in previous work on calf-thymus deoxyribonucleic acid. These results are summarised as follows :

Component	R_C	M_C †	Proposed structure *
Myco. phlei 4A	0·37	9·3	T–P–S–P
Calf-thymus 3A	0·35	9·1	
Myco. phlei 4B	0·37	6·8	C–P–S–P
Calf-thymus 3C	0·35	6·6	

* See Table 2. † M_C = Distance moved by component relative to distance moved by cytidylic acid (corrected for endosmosis).

Zone 2. This zone separated into 6 components by paper electrophoresis at pH 3·5. Components 2A and 2B corresponded in base content and R_C value (0·15) in propan-2-ol–ammonia with components from calf-thymus deoxyribonucleic acid identified as indicated in Table 2. Their behaviour on electrophoresis was consistent with these structures.

Zone 1. This was heterogeneous. No definite resolution was obtained either by two-dimensional paper electrophoresis or by electrophoresis in the Antweiler micro-electrophoresis apparatus.

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480. *Degradative Studies on Peptides and Proteins. Part IV.* The Formation of Salts of 2-Acylaminothiazol-5-ones by Acid-catalysed Degradation of N-Acylthiocarbamoylpeptides and their Behaviour towards Nucleophilic Reagents.*

By D. T. Elmore and (in part) P. A. Toseland.

N-Acylthiocarbamoylpeptides and their esters, under suitable conditions of acid catalysis, afford salts of 2-acylaminothiazol-5-ones. Nucleophilic reagents such as water, alcohols, and primary amines open the heterocyclic ring to give *N*-acylthiocarbamoylamino-acid derivatives, which have in most cases been identified by comparison with samples prepared by unambiguous routes. 2-Benzamidothiazol-5-one hydrochloride is converted into 1-benzoylthiocarbamoyl-2-thiohydantoin by reaction with ammonium thiocyanate.

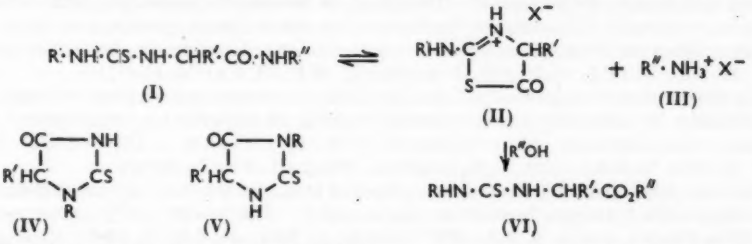
Recently, a new method of stepwise degradation of peptides was reported,[1] in which *N*-acylthiocarbamoylpeptides were subjected to mild acid treatment. The *N*-terminal amino-acid of the original peptide was recovered and identified as a 2-thiohydantoin. It was briefly mentioned that, if anhydrous acid catalysts were used, 3-acyl-2-thiohydantoins (V; R = Ac or Bz) were formed initially. Later work, however, has revealed that these products are in fact salts (II) of 2-acylaminothiazol-5-ones. Such compounds were prepared by Aubert, Knott, and Williams[2] by treatment of *N*-acylthiocarbamoylamino-acids with phosphorus tribromide in a mixture of dioxan and ether. These authors considered the alternative structure (IV), but rejected it because the latter would be expected to be stable, whereas their products were unstable in moist air and aqueous sodium acetate. In fact, the only reasonable structure not involving an acyl migration would be a 3-acyl-2-thiohydantoin (V). Such compounds, which may be regarded as *NN*-diacylthioamides, would almost certainly be attacked by nucleophilic reagents. Hence, the lability to bases of the compounds isolated by Aubert *et al.*[2] is no criterion of their structure. It is exceedingly unlikely, however, that 3-acyl-2-thiohydantoins (V) would be basic, since neither 2-thiohydantoins nor their 1-acyl derivatives are. On the other hand, thiazol-5-ones, like oxazol-5-ones, would be expected to be weak bases. Moreover, as Aubert *et al.*[2] indicated, electronic considerations suggest that nucleophilic attack by the sulphur atom at the electrophilic carbonyl-carbon atom giving 2-acylaminothiazol-5-ones is the more likely event. A similar mechanism is envisaged for the acid-catalysed degradation of *N*-acylthiocarbamoyl peptides, since protonation of the peptide linkage would increase the electrophilic character of the carbonyl-carbon atom. Very recently, Edman[3] has demonstrated that 2-anilinothiazol-5-ones (II; R = Ph) are the first products resulting from the acid-catalysed degradation of *N*-phenylthiocarbamoylpeptides (I; R = Ph). Kenner and Khorana[4] had earlier suggested that degradation of *N*-thioncarbalkoxypeptides in nitromethane saturated with dry hydrogen chloride afforded thiazolid-2 : 5-diones, although the instability of the latter unfortunately precluded rigid proof of structure. These observations corroborate our present view of the mechanism of acid-catalysed degradation of *N*-acylthiocarbamoylpeptides, but we decided to obtain definitive proof if possible.

Since acid-catalysed degradation of *N*-acylthiocarbamoylpeptides produces two salts (II and III), which frequently have similar solubilities, the isolation of the unstable 2-acylaminothiazol-5-one salts (II) in an analytically pure state has been difficult. Nevertheless, we successfully isolated 2-benzamidothiazol-5-one hydrochloride (II; R = Bz, R′ = H,

* Part III, *J.*, 1956, 192.

[1] Elmore and Toseland, *J.*, 1954, 4533.
[2] Aubert, Knott, and Williams, *J.*, 1951, 2185.
[3] Edman, *Nature*, 1956, **177**, 667; *Acta Chem. Scand.*, 1956, **10**, 761.
[4] Kenner and Khorana, *J.*, 1952, 2076.

X = Cl) after treatment of *N*-benzoylthiocarbamoylglycylglycine ethyl ester (I; R = Bz, R′ = H, R″ = CH_2·CO_2Et) with dry hydrogen chloride in nitromethane. Elementary analysis and comparison of its ultraviolet and infrared spectra with those of the corresponding hydrobromide made by the method of Aubert *et al.*[2] confirmed its structure. In addition, the hydrochloride was also obtained from *N*-benzoylthiocarbamoylglycine by the action of phosphorus trichloride in dioxan–ether and it had an identical infrared spectrum. In some cases it was possible to precipitate pure 2-acylamidothiazol-5-one salts from reaction mixtures of the *p*-toluidides of *N*-acylthiocarbamoylamino-acids (I; R″ = *p*-Me·C_6H_4) in acetic acid saturated with dry hydrogen chloride by careful addition of ether. By this method, the thiazol-5-one hydrochlorides (II; R = Ac, R′ = H and Me, X = Cl; and R = Bz, R′ = Me, X = Cl) were obtained. *N*-Benzoylthiocarbamoyl-DL-norleucine *p*-toluidide and -DL-phenylalanine *p*-toluidide (I; R = Bz,



R′ = Bu^n and Ph·CH_2, R″ = *p*-Me·C_6H_4), however, were rather resistant to degradation, probably as a result of steric hindrance, and the corresponding thiazol-5-ones could not be prepared from these compounds. Finally, *N*-acetyl- and *N*-2 : 4-dichlorobenzoylthiocarbamoylglycylglycine ethyl ester (I; R = Ac and $C_6H_3Cl_2$·CO, R′ = H, R″ = CH_2·CO_2Et) in trifluoroacetic acid afforded what are believed to be the 2-acylaminothiazol-5-one trifluoroacetates (II; R = Ac and $C_6H_3Cl_2$·CO, R′ = H, X = CF_3·CO_2) as amorphous powders. These could not be crystallised and did not give satisfactory analyses, but their reactions leave little doubt of their constitution.

Thiazol-5-ones would be expected to undergo ring-opening by nucleophilic reagents more readily than oxazol-5-ones, since the $+M$ effect of –SR is less than that of –OR. For example, Cook, Harris, Heilbron, and Shaw [5] found that 2-benzylthiothiazol-5-one hydrobromide afforded *N*-dithiobenzyloxycarbonylglycine benzylamide with benzylamine in the cold, and Jepson, Lawson, and Lawton [6] showed that 2-arylthiazol-5-ones were cleaved by a variety of bases. We have found that 2-acylaminothiazol-5-ones readily undergo ring-scission with a variety of nucleophilic reagents. Water and alcohols at elevated temperatures rapidly gave rise to *N*-acylthiocarbamoylamino-acids (VI; R″ = H) and their esters respectively, while amines reacted in the cold or on brief warming to give the corresponding amide derivative (I). Although Jepson *et al.*[6] reported that 2-arylthiazol-5-ones were unaffected by ammonium thiocyanate, we found that 2-benzamidothiazol-5-one hydrochloride (II; R = Bz, R′ = H, X = Cl) reacted smoothly to give a product, which is believed to be 1-benzoylthiocarbamoyl-2-thiohydantoin (IV; R = Bz·NH·CS, R′ = H), although we have not confirmed this by independent synthesis. Presumably, the thiazol-5-one ring was cleaved initially to give benzoylthioureidoacetyl *iso*thiocyanate, which then cyclised in the usual manner.[7] In view of the ease with which the thiazol-5-one ring can be opened, it is remarkable that Takahashi, Nishigaki, and Sakomoto [8] have reported that 2-acetamido-5-amino-4-propenylthiazole is converted into 2-acetamido-4-propenylthiazol-5-one by recrystallisation from ethanol.

[5] Cook, Harris, Heilbron, and Shaw, *J.*, 1948, 1056.
[6] Jepson, Lawson, and Lawton, *J.*, 1955, 1791.
[7] Johnson and Scott, *J. Amer. Chem. Soc.*, 1913, **35**, 1136.
[8] Takahashi, Nishigaki, and Sakomoto, *J. Pharm. Soc. Japan*, 1953, **73**, 1076; *Chem. Abs.*, 1954, **48**, 12082 h.

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In conclusion, it is worth recording that the method of peptide synthesis due to Anderson, Blodinger, and Welcher [9] has proved very suitable for converting *N*-acylthiocarbamoyl-amino-acids into amide derivatives.

Experimental

Infrared spectra were measured in pressed discs of potassium bromide with a Grubb-Parsons double-beam spectrometer and a rock-salt prism.

N-Benzyloxycarbonylglycine p-Toluidide.—This *compound* (57%) was prepared by using the mixed acid anhydride procedure of Vaughan *et al.*[10] Recrystallised from chloroform–light petroleum (b. p. 40—60°), it had m. p. 153—154° (Found: C, 67·9; H, 6·1; N, 9·4. $C_{17}H_{18}O_3N_2$ requires C, 68·4; H, 6·1; N, 9·4%).

Glycine p-Toluidide Hydrobromide.—Treatment of *N*-benzyloxycarbonylglycine *p*-toluidide with hydrogen bromide in acetic acid [11] afforded this *salt* in almost quantitative yield. After two recrystallisations from ethanol–ether, it softened and decomposed above 200° (Found: C, 43·5; H, 5·3; N, 11·3. $C_9H_{13}ON_2Br$ requires C, 44·1; H, 5·4; N, 11·4%).

N-Benzyloxycarbonyl-DL-alanine p-Toluidide.—This *compound* was prepared through mixed acid anhydrides by using ethyl chloroformate [10] (58%) or tetraethyl pyrophosphite [9] (96%). Crystallised from chloroform–light petroleum (b. p. 60—90°), it had m. p. 153·0—153·5° (Found: C, 69·3; H, 6·6; N, 8·9. $C_{18}H_{20}O_3N_2$ requires C, 69·2; H, 6·5; N, 9·0%).

DL-Alanine p-toluidide hydrobromide was prepared from the *N*-benzyloxycarbonyl derivative by treatment with hydrogen bromide in acetic acid.[11] The *product* (87%), after recrystallisation from ethanol, had m. p. 203—204° (Found: C, 46·1; H, 5·5; N, 10·6. $C_{10}H_{15}ON_2Br$ requires C, 46·3; H, 5·8; N, 10·8%).

N-Benzyloxycarbonyl-DL-phenylalanine p-toluidide was obtained in excellent yield by the pyrophosphite procedure of Anderson *et al.*[9] After recrystallisation from ethyl acetate–light petroleum (b. p. 40—60°) and then from chloroform, it had m. p. 157° (Found: C, 74·4; H, 6·4; N, 7·4. $C_{24}H_{24}O_3N_2$ requires C, 74·2; H, 6·2; N, 7·2%).

DL-Phenylalanine p-toluidide hydrobromide was obtained in almost theoretical yield by treatment of the foregoing compound with hydrogen bromide in acetic acid.[11] Three recrystallisations from ethanol–ether afforded the salt as a monohydrate, m. p. 210·0—210·5°, after previously melting at 119—121° and resolidifying above this temperature (Found: C, 54·4; H, 6·0; N, 7·9. $C_{16}H_{19}ON_2Br,H_2O$ requires C, 54·4; H, 6·0; N, 7·9%).

N-Benzyloxycarbonyl-DL-norleucine p-Toluidide.—The method of Anderson *et al.*[9] gave this compound in theoretical yield, m. p. 149·5—150·5° after recrystallisation from ethyl acetate–light petroleum (b. p. 60—90°) (Found: C, 71·1; H, 7·3; N, 7·8. $C_{21}H_{26}O_3N_2$ requires C, 71·2; H, 7·4; N, 7·9%).

DL-Norleucine p-Toluidide.—*N*-Benzyloxycarbonyl-DL-norleucine *p*-toluidide, in methanol containing a few drops of acetic acid, was hydrogenolysed over palladous oxide. After filtration and evaporation, the residue was partitioned between ethyl acetate and dilute hydrochloric acid. The aqueous layer was basified and extracted with ethyl acetate. *DL-Norleucine p-toluidide* (72%) crystallised from the dried extract after evaporation and addition of light petroleum (b. p. 40—60°); it had m. p. 63·5—64·0° (Found: C, 70·6; H, 9·1; N, 12·6. $C_{13}H_{20}ON_2$ requires C, 70·9; H, 9·1; N, 12·7%).

N-Benzyloxycarbonylglycine p-Benzyloxycarbonylanilide.—Reaction of *N*-benzyloxycarbonylglycine, benzyl *p*-aminobenzoate, and tetraethyl pyrophosphite in diethyl hydrogen phosphite at 95—100° for 1 hr.[9] afforded this *compound* in almost quantitative yield. After two recrystallisations from ethyl acetate–light petroleum (b. p. 40—60°), it had m. p. 144—145° (Found: C, 68·8; H, 5·5; N, 7·1. $C_{24}H_{22}O_5N_2$ requires C, 68·9; H, 5·3; N, 6·7%).

Glycine p-Carboxyanilide.—The foregoing compound (5·8 g.) was hydrogenolysed in methanol (150 c.c.) and dioxan (30 c.c.) over palladous oxide. The solution was filtered and the precipitate was leached with boiling water. The cooled extract deposited glycine *p*-carboxyanilide (2·2 g.), m. p. 240° (decomp.). A paper chromatogram of the product irrigated with butan-1-ol–acetic acid–water (4 : 1 : 5) revealed a single yellow spot when sprayed with 0·2% ninhydrin

[9] Anderson, Blodinger, and Welcher, *J. Amer. Chem. Soc.*, 1952, **74**, 5309.
[10] Vaughan and Osato, *ibid.*, p. 676.
[11] Ben-Ishai, *J. Org. Chem.*, 1954, **19**, 62.

in butan-1-ol (Found : C, 50·3; H, 5·7; N, 12·9. Calc. for $C_9H_{10}O_3N_2,H_2O$: C, 50·9; H, 5·7; N, 13·2%). King, Clark-Lewis, Kidd, and Smith [12] report m. p. 300° (decomp.) but Tropp [13] reports m. p. 229° (decomp.) for the monohydrate.

2-Benzamidothiazol-5-one Hydrochloride (II; R = Bz, R′ = H, X = Cl).—(*a*) Dry hydrogen chloride was blown through a suspension of *N*-benzoylthiocarbamoylglycylglycine ethyl ester (4 g.; prepared as before [1] in almost quantitative yield; m. p. 161·0—161·5° after softening at 155°) in dry nitromethane at 0°. During 2 hr., the starting material dissolved and was replaced by a precipitate of *2-benzamidothiazol-5-one hydrochloride* (2·25 g.), which was collected and dried *in vacuo* over phosphoric oxide and sodium hydroxide and then had m. p. 192—193° (decomp.) (Found : C, 46·5; H, 3·8; N, 11·3. $C_{10}H_9O_2N_2SCl$ requires C, 46·8; H, 3·5; N, 10·9%). Light absorption in methylene chloride : $\lambda_{max.}$ 2440 (ε 17,800). The filtrate from 2-benzamidothiazol-5-one hydrochloride deposited glycine ethyl ester hydrochloride (1·3 g.), m. p. 138—139°.

(*b*) This compound was also prepared from *N*-benzoylthiocarbamoylglycine by treatment with phosphorus trichloride in ether–dioxan [2] and had m. p. 190—192° (decomp.).

2-Benzamidothiazol-5-one hydrobromide, prepared as described by Aubert *et al.*,[2] had m. p. 206—207° (decomp.) (Found : C, 39·6; H, 3·3; N, 9·2. Calc. for $C_{10}H_9O_2N_2SBr$: C, 39·9; H, 3·0; N, 9·3%). Light absorption in methylene chloride : $\lambda_{max.}$ 2460—2480 (ε 17,100). The infrared spectra of the two samples of hydrochloride and the hydrobromide were severally identical.

N-Benzoylthiocarbamoylglycine.—2-Benzamidothiazol-5-one hydrochloride (20 mg.) was heated in boiling water (4 c.c.) for 5 min. On cooling, *N*-benzoylthiocarbamoylglycine (14 mg.) separated, having m. p. 202—203° alone or on admixture with an authentic sample. The infrared spectra of the two samples were identical.

N-Benzoylthiocarbamoylglycine Methyl Ester (VI; R = Bz, R′ = H, R″ = Me).—(*a*) This *ester* (67%) was prepared by the general method of Douglass and Dains.[14] Recrystallised from methanol, it had m. p. 98° (Found : C, 52·4; H, 4·9; N, 11·0; S, 12·5. $C_{11}H_{12}O_3N_2S$ requires C, 52·4; H, 4·8; N, 11·1; S, 12·7%).

(*b*) 2-Benzamidothiazol-5-one hydrochloride (100 mg.) was heated in methanol (10 c.c.) on the steam-bath for 5 min. The product, which separated after the addition of ether (10 c.c.), had m. p. 98° alone or in admixture with the foregoing specimen.

N-Benzoylthiocarbamoylglycine Ethyl Ester.—Ring-scission of 2-benzamidothiazol-5-one hydrochloride with ethanol afforded this compound (85%), m. p. 129° from ethanol–light petroleum (b. p. 40—60°). Mixed m. p. with an authentic sample was not depressed, and infrared spectra of the two specimens were identical.

N-Benzoylthiocarbamoylglycine cyclo*Hexylamide* (I; R = Bz, R′ = H, R″ = C_6H_{11}).—(*a*) A mixture of *N*-benzoylthiocarbamoylglycine (476 mg.), *cyclo*hexylamine (198 mg.), and tetraethyl pyrophosphite (542 mg.) in diethyl hydrogen phosphite (2 c.c.) was kept at 90° for 1 hr. The cyclo*hexylamide* (478 mg.), precipitated by addition of water, was recrystallised from ethanol three times and had m. p. 204—205° (Found : C, 60·2; H, 6·3; N, 12·7. $C_{16}H_{21}O_2N_3S$ requires C, 60·2; H, 6·6; N, 13·2%).

(*b*) To a solution of *cyclo*hexylamine (165 mg.) in chloroform (10 c.c.) was added 2-benzamidothiazol-5-one hydrochloride (360 mg.). The solution immediately darkened and, after being warmed for a few minutes, was shaken with charcoal, filtered, and washed successively with dilute hydrochloric acid, water, saturated sodium hydrogen carbonate, and water. After the solution was evaporated to dryness, the product (118 mg.), crystallised from ethanol, had m. p. 203·5—204·0°, undepressed by admixture with the above sample. The infrared spectra were identical.

1-Benzoylthiocarbamoyl-2-thiohydantoin (IV; R = Bz·NH·CS, R′ = H).—A mixture of 2-benzamidothiazol-5-one hydrochloride (1·4 g.) and dry ammonium thiocyanate (1·5 g.) in glacial acetic acid (25 c.c.) was heated on the steam-bath until dissolution was complete and was then poured into water (300 c.c.). The precipitate, recrystallised from ethyl acetate–light petroleum (b. p. 40—60°), afforded yellow *1-benzoylthiocarbamoyl-2-thiohydantoin* (0·92 g.), m. p. 189—192° (decomp.) (Found : C, 47·1; H, 3·7; N, 15·3; S, 22·9. $C_{11}H_9O_2N_3S_2$ requires C, 47·3; H, 3·3; N, 15·0; S, 23·0%).

[12] King, Clark-Lewis, Kidd, and Smith, *J.*, 1954, 1039.
[13] Tropp, *Ber.*, 1928, **61**, 1431.
[14] Douglass and Dains, *J. Amer. Chem. Soc.*, 1934, **56**, 719.

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2-Benzamido-4-methylthiazol-5-one Hydrochloride (II; R = Bz, R′ = Me, X = Cl).—A suspension of *N*-benzoylthiocarbamoyl-DL-alanine *p*-toluidide (300 mg.) (see below) in acetic acid (9 c.c.) saturated with dry hydrogen chloride was shaken for 1 hr. Dry ether (7 c.c.) was added to the clear solution; the precipitated *product* (150 mg.) had m. p. 187—189° (decomp.) (Found: C, 49·0; H, 4·3; N, 9·8. $C_{11}H_{11}O_2N_2SCl$ requires C, 48·8; H, 4·1; N, 10·4%).

N-*Benzoylthiocarbamoyl*-DL-*alanine* p-*Toluidide* (I; R = Bz, R′ = Me, R″ = *p*-C_6H_4Me).—(*a*) This *compound* was obtained from DL-alanine *p*-toluidide by reaction with either benzoyl *iso*thiocyanate in ether (92%) or methyl *N*-benzoyldithiocarbamate in ethanol–ether (89%). Recrystallised from ethanol, it had m. p. 207·0—207·5° (Found: C, 63·0; H, 5·7; N, 12·4. $C_{18}H_{19}O_2N_3S$ requires C, 63·3; H, 5·6; N, 12·3%).

(*b*) 2-Benzamido-4-methylthiazol-5-one hydrochloride (167 mg.) and *p*-toluidine (66 mg.) in warm chloroform (5 c.c.) were allowed to react for a few minutes. Addition of light petroleum (b. p. 40—60°) to the cooled and filtered solution afforded *N*-benzoylthiocarbamoyl-DL-alanine *p*-toluidide (86 mg.), m. p. 207·5° after recrystallisation from ethanol and on admixture with the above product. Infrared spectra of the two specimens were identical.

N-*Benzoylthiocarbamoyl*-DL-*alanine* (VI; R = Bz, R′ = Me, R″ = H).—(*a*) Reaction of methyl *N*-benzoyldithiocarbamate with DL-alanine afforded N-*benzoylthiocarbamoyl*-DL-*alanine* (74%), which separated from ethanol with one molecule of solvent of crystallisation, then having 144° (Found: C, 52·7; H, 6·0; N, 9·4. $C_{11}H_{12}O_3N_2S,C_2H_5OH$ requires C, 52·3; H, 6·1; N, 9·4%). After drying at 120°/0·05 mm. for 6 hr., it had m. p. 157° (Found: C, 52·4; H, 4·5; N, 11·0. $C_{11}H_{12}O_3N_2S$ requires C, 52·4; H, 4·8; N, 11·1%).

(*b*) Dissolution of 2-benzamido-4-methylthiazol-5-one hydrochloride in boiling water followed by cooling afforded the above compound (92%), m. p. 155—157°. This specimen did not depress the m. p. of that prepared as above and had an identical infrared spectrum.

N-*Benzoylthiocarbamoyl*-DL-*alanine Ethyl Ester* (VI; R = Bz, R′ = Me, R″ = Et).—This ester (77%), which resulted from the action of hot ethanol on 2-benzamido-4-methylthiazol-5-one hydrochloride, had m. p. 121°, undepressed on admixture with an authentic sample.[1] Comparison of infrared spectra confirmed their identity (Found: C, 55·8; H, 5·7; N, 10·2; S, 11·9. Calc. for $C_{13}H_{16}O_3N_2S$: C, 55·7; H, 5·8; N, 10·0; S, 11·4%).

N-2 : 4-*Dichlorobenzoylthiocarbamoylglycylglycine Ethyl Ester* (I; R = $C_6H_3Cl_2$·CO, R′ = H, R″ = CH_2·CO_2Et).—Reaction of methyl *N*-2 : 4-dichlorobenzoyldithiocarbamate [15] with glycyl-glycine ethyl ester in chloroform at room temperature during 2 days afforded this *ester* (77%), m. p. 206·5—207·0° (decomp.) after recrystallisation from propan-1-ol (Found: C, 43·0; H, 4·2; N, 10·3; S, 7·8. $C_{14}H_{15}O_4N_3SCl_2$ requires C, 42·9; H, 3·9; N, 10·7; S, 8·2%).

2-(2 : 4-*Dichlorobenzamido*)*thiazol-5-one Trifluoroacetate* (II; R = $C_6H_3Cl_2$·CO, R′ = H, X = CF_3·CO_2).—*N*-2 : 4-Dichlorobenzoylthiocarbamoylglycylglycine ethyl ester (1 g.) was left in trifluoroacetic acid (5 c.c.) for 4 hr. at room temperature. The solution was poured into dry ether (200 c.c.) and left for 15 min. at 0°. A crystalline precipitate (presumably glycine ethyl ester trifluoroacetate, although satisfactory analyses could not be obtained), m. p. 136·0—137·5°, was removed and the filtrate was evaporated under reduced pressure to 50 c.c. Addition of light petroleum (b. p. 40—60°) precipitated, after 15 min. at 0°, the thiazol-5-one salt as a light brown, amorphous solid, which was used for the reactions described below.

N-2 : 4-*Dichlorobenzoylthiocarbamoylglycine Ethyl Ester* (VI; R = $C_6H_3Cl_2$·CO, R′ = H, R″ = Et).—(*a*) Reaction of methyl *N*-2 : 4-dichlorobenzoyldithiocarbamate with glycine ethyl ester in chloroform produced N-2 : 4-*dichlorobenzoylthiocarbamoylglycine ethyl ester* (50%), m. p. 145·5—146·5° after recrystallisation from carbon tetrachloride (Found: C, 43·1; H, 3·9; N, 8·1; Cl, 21·5. $C_{12}H_{12}O_3N_2SCl_2$ requires C, 43·0; H, 3·6; N, 8·4; Cl, 21·2%).

(*b*) 2-(2 : 4-Dichlorobenzamido)thiazol-5-one trifluoroacetate in refluxing ethanol afforded the above ester (45%), m. p. 142·5—143·5° after recrystallisation. The infrared spectra of the two samples were identical.

N-2 : 4-*Dichlorobenzoylthiocarbamoylglycine* (VI; R = $C_6H_3Cl_2$·CO, R′ = R″ = H).—(*a*) Reaction of methyl *N*-2 : 4-dichlorobenzoyldithiocarbamate with glycine in 67% aqueous dioxan at pH 8·8 and 37° during 5·25 hr., followed by isolation in the usual way,[1] afforded the desired *compound* (91%), m. p. 197·5—199·0° (decomp.) after recrystallisation from ethanol–light petroleum (b. p. 40—60°) (Found: C, 39·0; H, 2·8; S, 10·7. $C_{10}H_8O_3N_2SCl_2$ requires C, 39·1; H, 2·6; S, 10·4%).

[15] Elmore, Ogle, Fletcher, and Toseland, *J.*, 1956, 4458.

(*b*) A solution of 2-(2 : 4-dichlorobenzamido)thiazol-5-one trifluoroacetate in refluxing 25% aqueous dioxan gave, after decantation from tar, the same compound (37%), m. p. 193—195° (decomp.), raised after recrystallisation to 197·0—197·5° (decomp.) alone or on admixture with the above sample. Infrared spectra of the two specimens were identical.

N-2 : 4-*Dichlorobenzoylthiocarbamoylglycine* p-*Carboxyanilide* (I; R = $C_6H_3Cl_2$·CO, R′ = H, R″ = *p*-C_6H_4·CO_2H).—Brief warming of a mixture of 2-(2 : 4-dichlorobenzamido)thiazol-5-one trifluoroacetate and *p*-aminobenzoic acid in chloroform–dioxan (2 : 1) gave the desired *product* (82%). After recrystallisation from aqueous dioxan then from pyridine–benzene, it had m. p. 260—261° (decomp.) (Found: C, 48·1; H, 3·1; N, 10·3. $C_{17}H_{12}O_4N_2SCl_2$ requires C, 47·9; H, 3·1; N, 9·9%).

2-*Acetamidothiazol-5-one Hydrochloride* (II; R = Ac, R′ = H, X = Cl).—(*a*) *N*-Acetylthiocarbamoylglycine *p*-toluidide (265 mg.) was degraded in acetic acid (10 c.c.) saturated with hydrogen chloride. Addition of dry ether (8 c.c.) precipitated the *product* (94 mg.), m. p. 176° (decomp.) after darkening from about 160° (Found: C, 31·1; H, 4·0; N, 14·0. $C_5H_7O_2N_2SCl$ requires C, 30·8; N, 3·6; N, 14·4%).

(*b*) Treatment of *N*-acetylthiocarbamoylglycine in ether–dioxan with phosphorus trichloride also afforded the desired compound (84%), m. p. 178—183° (decomp.) after darkening from about 160°. Infrared spectra of the two specimens were identical. This compound was very unstable; after storage in a desiccator for 3 weeks, infrared spectroscopy showed that it had completely reverted to *N*-acetylthiocarbamoylglycine.

2-*Acetamidothiazol-5-one Trifluoroacetate* (II; R = Ac, R′ = H, X = CF_3·CO_2).—*N*-Acetylthiocarbamoylglycylglycine ethyl ester (the m. p. of this compound is 166°, not 112° as reported earlier [1]), degraded in trifluoroacetic acid as described for the *N*-2 : 4-dichlorobenzamido-analogue, afforded 2-acetamidothiazol-5-one trifluoroacetate, m. p. 105—106°. Satisfactory analytical results could not be obtained on this substance, probably because of rapid loss of trifluoroacetic acid (cf. Aubert *et al.*[3]). In consequence, the yields of products derived through ring-opening reactions are not significant and are not given. Treatment with hot water and hot ethanol respectively afforded *N*-acetylthiocarbamoylglycine, m. p. 200—202°, and its ethyl ester, m. p. 105°. Comparison of infrared spectra with those of authentic specimens confirmed their identities.

N-*Acetylthiocarbamoylglycine* p-*Toluidide* (I; R = Ac, R′ = H, R″ = *p*-C_6H_4Me).—(*a*) A mixture of *N*-acetylthiocarbamoylglycine (220 mg.), *p*-toluidine (107 mg.), and tetraethyl pyrophosphite (300 mg.) in diethyl hydrogen phosphite (6 c.c.) was kept at 90° for 30 min. and then poured into water.[9] The precipitated *product* (280 mg.), after recrystallisation from ethanol, had m. p. 237—239° (decomp.) (Found: C, 54·5; H, 5·7; N, 15·8. $C_{12}H_{15}O_2N_3S$ requires C, 54·3; H, 5·7; N, 15·8%).

(*b*) Reaction of 2-acetamidothiazol-5-one trifluoroacetate with *p*-toluidine in warm chloroform also afforded this compound, m. p. 237—239° (decomp.), undepressed by admixture with the above sample. Infrared spectra were identical.

N-*Acetylthiocarbamoylglycine* p-*Ethoxycarbonylanilide* (I; R = Ac, R′ = H, R″ = *p*-C_6H_4·CO_2Et).—(*a*) A mixture of *N*-acetylthiocarbamoylglycine (350 mg.), ethyl *p*-aminobenzoate (330 mg.), and tetraethyl pyrophosphite (520 mg.) in diethyl hydrogen phosphite (3 c.c.) was kept at 100—110° for 1 hr.[9] Addition of water to the cooled mixture furnished the *product* (550 mg.), m. p. 226—227° (decomp.), unaltered by recrystallisation from ethanol–chloroform–light petroleum (b. p. 60—90°) (Found: C, 51·5; H, 5·5; N, 13·0; S, 10·1. $C_{14}H_{17}O_4N_3S$ requires C, 52·0; H, 5·3; N, 13·0; S, 9·9%).

(*b*) The above compound was also obtained on reaction between 2-acetamidothiazol-5-one trifluoroacetate and ethyl *p*-aminobenzoate in chloroform. The recrystallised sample had m. p. 226° (decomp.), undepressed on admixture with the above specimen, and had an identical infrared spectrum.

N-*Acetylthiocarbamoyl* p-*Carboxyanilide* (I; R = Ac, R′ = H, R″ = *p*-C_6H_4·CO_2H).—(*a*) Interaction of glycine *p*-carboxyanilide (640 mg.) and methyl *N*-acetyldithiocarbamate (895 mg.) in 67% aqueous dioxan at pH 9·0 and 37° furnished N-*acetylthiocarbamoylglycine* p-*carboxyanilide* (660 mg.), m. p. 260—262° (decomp.) after recrystallisation from pyridine–benzene (Found: C, 48·8; H, 4·4; N, 14·4. $C_{12}H_{12}O_4N_2S$ requires C, 48·8; H, 4·2; N, 14·2%).

(*b*) Reaction of 2-acetamidothiazol-5-one trifluoroacetate with *p*-aminobenzoic acid in dry dioxan at room temperature overnight also afforded this compound, m. p. 260° (decomp.) after recrystallisation. The two specimens had identical infrared spectra.

XUM

N-*Acetylthiocarbamoyl*-DL-*alanine* p-*Toluidide* (I; R = Ac, R′ = Me, R″ = *p*-C_6H_4Me).—Reaction of DL-alanine *p*-toluidide and methyl *N*-acetyldithiocarbamate in ethanol–ether (4 : 1) at room temperature gave this *compound* (93%), m. p. 218° after recrystallisation from ethanol (Found: C, 56·1; H, 5·9; N, 15·2; S, 11·4. $C_{13}H_{17}O_2N_3S$ requires C, 55·9; H, 6·1; N, 15·0; S, 11·5%).

2-*Acetamido*-4-*methylthiazol*-5-*one Hydrochloride* (II; R = Ac, R′ = Me, X = Cl.)—(*a*) *N*-Acetylthiocarbamoyl-DL-alanine *p*-toluidide (279 mg.) was degraded in acetic acid (10 c.c.) saturated with dry hydrogen chloride. After addition of ether (8 c.c.), the *product* (43 mg.) crystallised overnight at 0°, and had m. p. 144—148° (decomp.) (Found: 34·3; H, 4·3; N, 13·3. $C_6H_9O_2N_2SCl$ requires C, 34·5; H, 4·4; N, 13·4%).

(*b*) Reaction of *N*-acetylthiocarbamoyl-DL-alanine with phosphorus trichloride in ether–dioxan also furnished this compound (76%), m. p. 147—149° (decomp.) (Found: C, 34·2; H, 4·8; N, 13·1%). The two specimens had identical infrared spectra.

N-*Benzoylthiocarbamoyl*-DL-*phenylalanine* p-*Toluidide* (I; R = Bz, R′ = $Ph{\cdot}CH_2$, R″ = *p*-C_6H_4Me).—Prolonged reaction of methyl *N*-benzoyldithiocarbamate and DL-phenylalanine *p*-toluidide in chloroform at room temperature gave only 58% of the theoretical yield of this *compound*. After recrystallisation from ethanol, it had m. p. 176·0—176·5° (Found: C, 68·9; H, 5·8; N, 10·1; S, 8·2. $C_{24}H_{23}O_2N_3S$ requires C, 69·0; H, 5·6; N, 10·1; S, 7·7%).

N-*Benzoylthiocarbamoyl*-DL-*norleucine* p-*Toluidide* (I; R = Bz, R′ = Bu^n, R″ = *p*-C_6H_4Me).—Prepared from DL-norleucine *p*-toluidide and methyl *N*-benzoyldithiocarbamate, this *compound* (85%) had m. p. 179·0—179·5° after recrystallisation from ethanol–light petroleum (b. p. 60—90°) (Found: C, 65·9; H, 6·9; N, 10·8. $C_{21}H_{25}O_2N_3S$ requires C, 65·8; H, 6·6; N, 11·0%).

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481. *Conjugated Macrocycles. Part XXIX.* Tribenzotetrazaporphin Metal Derivatives and Dibromotribenzotetrazaporphin.*

By J. A. ELVIDGE, J. H. GOLDEN, and R. P. LINSTEAD.

The preparation and purification of tribenzotetrazaporphin have been considerably improved. A contaminant is tentatively identified as monobenzotetrazaporphin.

Tribenzotetrazaporphin has been converted into the copper, nickel, and cobalt derivatives, and brominated to dibromotribenzotetrazaporphin (III). Oxidation of the last yields phthalimide and dibromomaleimide.

Light absorptions are given and commented upon.

DISCUSSION of the ways in which imidines might interact, with elimination of ammonia, to give tetrazaporphins, led two of us [1] to condense di-imino*iso*indoline with succinimidine. This reaction gave tribenzotetrazaporphin (I), the first unsymmetrically substituted tetrazaporphin to be isolated and characterised. Further studies have made the pure pigment more accessible, and we have converted it into metal derivatives (II) and the dibromo-derivative (III). The formation of these derivatives, and degradation of the dibromo-compound to phthalimide and dibromomaleimide, provide additional support for the macrocyclic structure (I) deduced earlier for the royal-blue pigment.

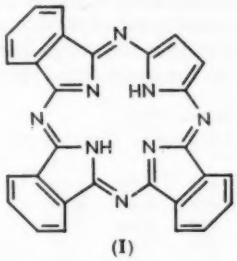
The disadvantage of the preparation of tribenzotetrazaporphin from imidines was the concomitant formation of three times the amount of phthalocyanine. Because of the similiarity of the two pigments, the isolation was lengthy, involving systematic extraction (to afford initial enrichment) and three stages of chromatography. Attempts to separate

* Part XXVIII, *J.*, 1957, 700.

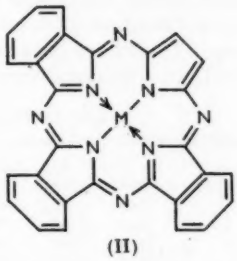
[1] Elvidge and Linstead, *J.*, 1955, 3536.

the pigments by other methods, and to prepare tribenzotetrazaporphin from other starting materials, gave no useful results.

A major improvement came from a reconsideration of our earlier generalisations.[1] Evidently some component of the di-imino*iso*indoline–succinimidine reaction mixture was acting as a hydrogen donor for the conversion of di-imino*iso*indoline into phthalocyanine;



(I)

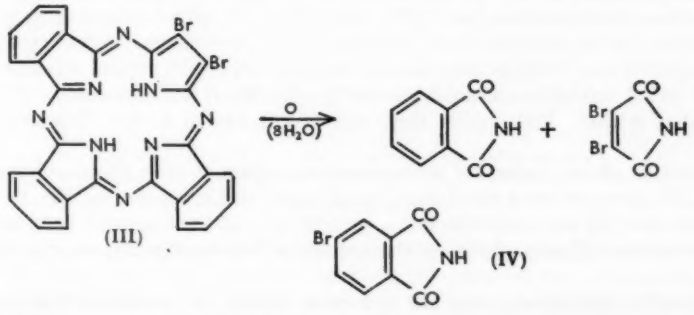


(II)

this was probably the succinimidine; it was not the solvent, ethanol, because its replacement by *tert.*-butanol had no effect. As competitors for the available hydrogen in the system, sodium chlorate and maleic acid were most effective. The tribenzotetrazaporphin was then obtained (in undiminished yield) contaminated with less than two-thirds of its weight of phthalocyanine. After an extractive crystallisation, the contamination was sufficiently small for the chromatography [1] to be modified and much larger throughputs were attained. Most of the phthalocyanine was adsorbed on tartaric acid (at higher proportions it is washed through the column) and the last traces were removed by chromatography on deactivated alumina in exceptionally short columns, the method obviating irreversible adsorption of tribenzotetrazaporphin.[1] It was then possible for one worker to obtain 200 mg. of the pigment in 3 weeks, compared with the 7—8 weeks previously needed for accumulation of 10—20 mg.

Metal Derivatives (II).—In boiling *o*-dichlorobenzene with copper bronze, anhydrous cobalt acetate, and Raney nickel, the pigment was converted into the copper, cobalt, and nickel derivatives, $C_{28}H_{14}N_8M$. Thus there are two replaceable hydrogen atoms in the molecule, $C_{28}H_{16}N_8$. The evidence [1] for the structure (I) was then complete.

Dibromo-compound (III).—The molecule of tribenzotetrazaporphin contains one pyrrole ring in which the two β-positions are free. Consequently it was expected that the pigment



(III)

would undergo electrophilic substitution: in fact bromination occurred readily in chlorobenzene at room temperature, a contrast to the behaviour of phthalocyanine,[2] and a stable dibromotribenzotetrazaporphin, $C_{28}H_{14}N_8Br_2$, was obtained, whose structure (III) was confirmed by degradation. Oxidation in concentrated sulphuric acid provided a mixture

[2] Barrett, Bradbrook, Dent, and Linstead, *J.*, 1939, 1820.

containing imides, separated by paper chromatography and identified as phthalimide and dibromomaleimide. No other imide was detected, and in particular the absence of 4-bromophthalimide (IV) was proved. These results are compatible only with the structure (III) and so with (I) for the parent pigment.

The 4-bromophthalimide, required as a marker in the paper chromatography, was prepared by an unambiguous route from 4-nitrophthalimide rather than by Waldmann's method.[3] Dunlap's method [4] for dibromomaleimide required modification.

Light Absorptions.—These have been determined for the metal derivatives (II) and the dibromo-pigment (III), in *o*-dichlorobenzene over the range 320—1000 mμ (see Table and

Light absorption characteristics.

(The full curves make certain peaks appear as minor ones : these are given in parentheses.)

	$\lambda_{max.}$ (mμ)				$\log_{10}\varepsilon$				Solvent
Tribenzotetrazaporphin ...	349	(566)	594	675	4·77	4·36	4·84	4·89 [1]	A
Cu ,, ...	349	(574)	630	663	4·83	4·38	4·94	4·94	B
Ni ,, ...	343	(566)	623	655	4·64	4·31	4·90	4·84	B
Co ,, ...	319	(567)	625	658	4·64	4·26	4·67	4·61	B
Dibromo- ,, ...	347	597	656	682	4·80	4·62	4·65	4·82	B
Phthalocyanine	350	(602, 638)	665	698	4·74	4·43 4·62	5·18	5·21	C *
Cu ,, ...	350	(611, 648)	679		4·76	4·56 4·51	5·34		C †
Ni ,, ...	(327) 350	(604, 643)	670		4·29 4·57	4·51 4·54	5·32		C †
Co ,, ...	348	(606)	672		4·65	4·53	5·19		C †
Tetrazaporphin	333		545	617	4·70		4·60	4·75 [6]	A
Cu ,, ...	334	(531)	578		4·57	4·13	4·98 [6]		B
Ni ,, ...	314 345	(530)	577		4·44 4·57	4·20	4·85 [6]		B

Solvents : A, chlorobenzene; B, *o*-dichlorobenzene; C, 1-chloronaphthalene.

* Dr. M. Whalley } Recent determinations on pure samples in these laboratories.
† Dr. G. E. Ficken }

Fig. 1). The general form of the absorption curve for tribenzotetrazaporphin (I) is similar to that of tetra*cyclo*hexenotetrazaporphin [5] or tetrazaporphin itself [6] (see ref. 1), but the spacing between the two main bands in the visible is rather larger (81 mμ) than that for all the other tetrazaporphins so far prepared, which show an interval of about 70 mμ.

The metallic derivatives of tribenzotetrazaporphin show two bands in the visible region, of similar intensity to one another and to those for the metal-free pigment, but 33 mμ apart. The spectra are thus unusual because in the other tetrazaporphins metallation results in replacement of the two main bands in the visible by an intense absorption peak, almost midway between them (see Table; also refs. 5, 7), which is accompanied by one or two subsidiary peaks at shorter wave-lengths. Another difference is that nickel tribenzotetrazaporphin shows a single maximum in the near-ultraviolet region, whereas previously examined nickel derivatives of (symmetrically) substituted tetrazaporphins show a double peak in that region. Presumably these effects are related to the dissymmetry of the molecule (I).

Substitution of the nucleus of tribenzotetrazaporphin to give dibromotribenzotetrazaporphin (III) gives rise to a third sharp peak in the visible region (see Fig. 1). No close comparisons for this are available, but a complication in the spectrum is to be expected, judging from the difference between the spectra of tribenzotetrazaporphin and phthalocyanine.

Monobenzotetrazaporphin.—In our previous work on tribenzotetrazaporphin we encountered a persistent contaminant, characterised by absorption bands at *ca.* 640 and 590 mμ, which was separated on a kieselguhr column as a mauve band.[1] Solutions of this

[3] Waldmann, *J. prakt. Chem.*, 1930, **126**, 65.
[4] Dunlap, *Amer. Chem. J.*, 1896, **18**, 332.
[5] Ficken and Linstead, *J.*, 1952, 4846.
[6] Linstead and Whalley, *J.*, 1952, 4839.
[7] Baguley, France, Linstead, and Whalley, *J.*, 1955, 3521.

pigment were reddish-blue and showed a red fluorescence which became bright pink in ultraviolet light. The same pigment was present in small amount in the mother-liquors from tribenzotetrazaporphin in our present work.

FIG. 1. *Absorption of (A) nickel tribenzotetrazaporphin (in o-$C_6H_4Cl_2$), (B) dibromotribenzotetrazaporphin (in o-$C_6H_4Cl_2$), and (C) tribenzotetrazaporphin (in* PhCl).

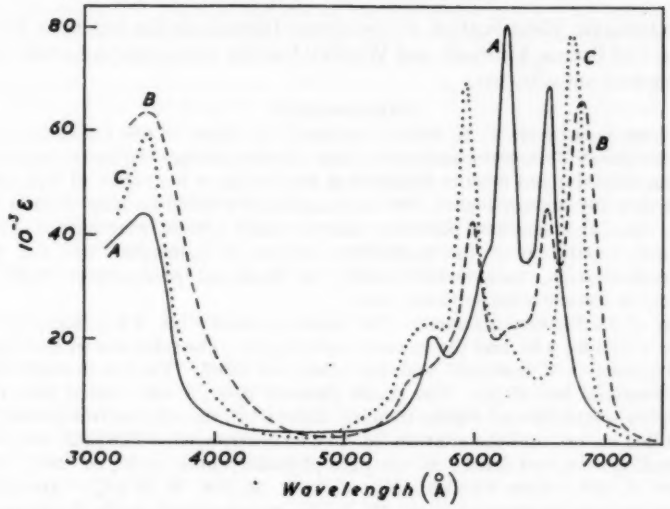
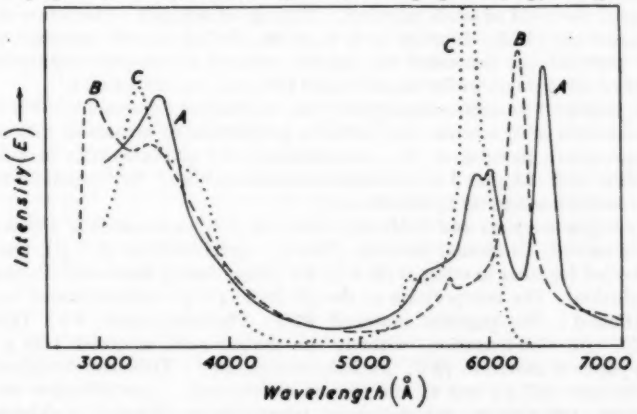


FIG. 2. *Absorption of (A) monobenzotetrazaporphin (in* PhCl), *(B) metal (?* Mg) *monobenzotetrazaporphin (in* PhCl), *and (C) magnesium tetrazaporphin [a] (in pyridine).*



The material from the accumulated solutions was chromatographed in chlorobenzene on kieselguhr, as before, and the tribenzotetrazaporphin removed as a fast-running blue band (1). This was followed by a mauve band of the new pigment (2). On continued elution, a small light blue band (3) and then a green band (4) passed down. Spectroscopic examination and acid treatment indicated that the traces of material were (3) a mixture of the new pigment with a heavy-metal tribenzotetrazaporphin, and (4) an alkaline-earth metal derivative of the new pigment. The light-absorption curve for the last was undoubtedly that of a new, pure, metallic tetrazaporphin (see Fig. 2). On acid treatment the absorption spectrum changed to that of fraction (2). Hence this solution was that of

a new metal-free tetrazaporphin, and the unusual doublet at 590—600 mμ was therefore authentic and not caused by a contaminant. A plot of $\lambda_{max.}$ of the longest-wavelength band against the number of benzene rings, for tetrazaporphin, tribenzotetrazaporphin, and phthalocyanine, indicated that the new pigment ($\lambda_{max.}$ 641 mμ) was *mono*benzotetrazaporphin. The fluorescence, which is reminiscent of that of tetrazaporphin, suggested the same.

This spectroscopic identification of monobenzotetrazaporphin has been made certain by recent work of Brown, Linstead, and Whalley [8] on the tetrazaporphins with methyl and fused-benzene-ring substituents.

Experimental

Microanalyses were by Mr. F. H. Oliver and Miss J. Cuckney of this Department.

Attempts to separate Tribenzotetrazaporphin from Phthalocyanine.—(i) Interaction of di-imino-*iso*indoline, succinimide, and lithium butoxide in butanol gave a mixture of lithium pigments, easily soluble in many organic liquids, but chromatography failed because of demetallation on the columns. (ii) The magnesium pigments, likewise easily soluble, were formed only in traces. (iii) Satisfactory separation of the metal-free mixture of pigments [1] was not effected by extractive crystallisation, vacuum-sublimation, or fractional precipitation from 80—100% phosphoric acid or concentrated sulphuric acid.

Estimation of the Pigment Mixtures.—The crude pigment [1] (*ca.* 0·6 g. sample) was stirred with 75% acetic acid for 5 hr. and the mixture centrifuged. The solid was washed by centrifugation with 75% acetic acid, methanol, and then ether, and dried. The loss in weight represented non-pigment material (*ca.* 73%). The crude pigment (0·6 g.) was dusted into stirred concentrated sulphuric acid (30 c.c.) during 15 min. After 2 hr., the solution was poured on crushed ice (from distilled water), and the mixture (*ca.* 75 c.c.) centrifuged. The solid was washed with water by centrifugation and dried: it was pure phthalocyanine (yield, *ca.* 20%) (Found: C, 74·7; H, 3·8; N, 21·7. Calc. for $C_{32}H_{16}N_8$: C, 74·7; H, 3·5; N, 21·8%). By difference the tribenzotetrazaporphin content was *ca.* 7%. The spectroscopic method—measurement of extinctions at 594 and 698 mμ (in PhCl solution)—confirmed the result.

*Condensation of Di-imino*iso*indoline with Succinimidine* (cf. ref. 1).—Dilution of the reaction mixture decreased the yield of crude pigment. Passage of nitrogen to facilitate the removal of ammonia increased the yield. Increase in b. p. of the alcohol solvent increased somewhat the yield of crude pigment but decreased the relative content of tribenzotetrazaporphin. Basic solvents offered no advantage, whilst in acetic acid pigment was not formed.

Attempts to prepare Tribenzotetrazaporphin from Alternative Compounds.—No useful results came from interaction of (i) succinic and phthalic anhydrides or nitriles in molten urea in the presence of ammonium molybdate, (ii) succinimidine and phthalonitrile in boiling ethanol, (iii) succinimidine and 1-imino-3-morpholino*iso*indolenine,[9] and (iv) di-imino*iso*indoline and diethyl succindi-imidoate and its hydrochloride.[10]

*Effect of Hydrogen-acceptors and Oxidising Agents on the Condensation of Di-imino*iso*indoline with Succinimidine.*—(i) Di-imino*iso*indoline (3·14 g.), succinimidine (0·7 g.), and maleic acid (0·25 g.) were boiled together in ethanol (20 c.c.) for 15 hr., during which dry nitrogen was passed through the solution. The composition of the product (1·7 g.) was estimated by the method given above (Found: Non-pigment material, 87·7; Phthalocyanine, 4·6; Tribenzotetrazaporphin, 7·7%). (ii) Condensation, without the maleic acid, afforded 1·63 g. of product (Found: Non-pigment material, 72·5; Phthalocyanine, 20·7; Tribenzotetrazaporphin, 6·8%). (iii) Sodium chlorate (0·3 g.) was as effective as maleic acid. Less effective were *m*-dinitrobenzene > sodium perchlorate, nitrobenzene, triethylamine *N*-oxide > chloranil. Di-*tert.*-butyl peroxide was ineffective. With benzoyl peroxide and lead tetra-acetate, no pigment was formed.

Tribenzotetrazaporphin (cf. ref. 1).—(a) *Formation.* Di-imino*iso*indoline (9·42 g.), succinimidine (2·1 g.), and sodium chlorate (0·9 g.) were boiled together in dry ethanol (50 c.c.) for 24 hr., whilst dry nitrogen was passed through the solution. The product (4·07 g.) was washed thoroughly with 75% acetic acid and then ethanol, and the residue was dried, powdered, and extracted continuously with benzene to yield crude tribenzotetrazaporphin (0·95 g.).

[8] Brown, Linstead, and Whalley, unpublished work.
[9] Clark, Elvidge, and Golden, *J.*, 1956, 4135.
[10] Pinner, *Ber.*, 1883, **16**, 352.

(b) *Chromatography.* (i) A filtered chlorobenzene solution of a portion of the crude pigment (15 mg./l.) was run continuously on to a column (8 × 40 cm.) of tartaric acid hydrate (B.P.; Hopkin & Williams, Ltd.). Some phthalocyanine washed through (in *ca.* 3 l.), followed by tribenzotetrazaporphin (at about the original concentration) contaminated with a trace of phthalocyanine. Most of the phthalocyanine was adsorbed as a green band, and the column was run until this extended nearly to the bottom (after 50 l.). The column was then washed with chlorobenzene (3 l.). (ii) 4-L. batches of the tribenzotetrazaporphin eluate (11·4 mg./l.; 53 l.) were run on to separate columns (6 cm. diam. × 1 cm.) of alumina (Spence, type H, deactivated to Brockmann grade IV [11] with 10% of water [12]). [Each alumina column, packed dry, was supported in a chromatogram tube on a filter-paper disc resting on silver sand. A paper disc protected the upper surface of the alumina.] Tribenzotetrazaporphin was retained on the alumina whilst the phthalocyanine passed through. *Without delay*, each column was washed with chlorobenzene (0·5—1·5 l.) and then eluted with chlorobenzene (1·5—3 l.) containing 5% of ethanol. 12-L. batches of the ethanolic eluates were filtered and distilled to 50 c.c., and the concentrates kept overnight. The small dark blue needles (total yield, 430 mg.) were free from phthalocyanine but contained a trace of a related pigment ($\lambda_{max.}$ *ca.* 640, 590 mμ). Extractive crystallisation of 50—100 mg. portions gave tribenzotetrazaporphin (average recovery, 87%) (Found: C, 72·6; H, 4·0; N, 24·2. Calc. for $C_{28}H_{16}N_8$: C, 72·4; H, 3·5; N, 24·1%).

Before conversion into derivatives, the pigment was chromatographed on kieselguhr,[1] but was found to be pure.

Chlorobenzene which contained unwanted pigment was recovered by filtration through a column (6 cm. diam × 3 cm.) of alumina–charcoal (5 : 1 by vol.) supported on alumina (6 cm.). Ethanolic chlorobenzene was washed continuously with water for 24 hr., and then run through a similar column surmounted by calcium chloride (3—8 mesh; 10 cm.).

Metal Derivatives of Tribenzotetrazaporphin.—Tribenzotetrazaporphin (67 mg.), copper bronze (1·5 g.), and *o*-dichlorobenzene (30 c.c.) were heated together under reflux for 5 hr. Next day, the solid was collected and extracted (Soxhlet) with chlorobenzene, to yield *copper tribenzotetrazaporphin* (51 mg.), which formed fine dark blue needles after extractive recrystallisation from chlorobenzene (Found: C, 64·0; H, 3·1; N, 21·4; Cu, 12·1. $C_{28}H_{14}N_8Cu$ requires C, 63·9; H, 2·7; N, 21·3; Cu, 12·1%).

Tribenzotetrazaporphin (42·7 mg.) was extracted into a suspension of anhydrous cobalt acetate (1·5 g.) in boiling *o*-dichlorobenzene (50 c.c.), and after 5 hr. the mixture was allowed to cool. Next day, the solid was washed well with 10% acetic acid, ethanol, and ether, and the residue extractively crystallised from chlorobenzene, to give *cobalt tribenzotetrazaporphin* (41·3 mg.) as dark blue needles (Found: C, 64·6; H, 3·0; N, 20·9; Co, 11·1. $C_{28}H_{14}N_8Co$ requires C, 64·5; H, 2·7; N, 21·5; Co, 11·3%).

o-Dichlorobenzene (35 c.c.), containing Raney nickel (1 g.), was boiled for 5 hr. in an extractor, the thimble of which contained tribenzotetrazaporphin (50 mg.). The extract mixture was kept overnight and then the solid was extracted with chlorobenzene for 30 hr., and the *nickel tribenzotetrazaporphin* (20·6 mg.) was extractively recrystallised from chlorobenzene to give dark blue needles with a lavender reflex (Found: C, 64·7; H, 3·2; N, 22·0; Ni, 10·2. $C_{28}H_{14}N_8Ni$ requires C, 64·5; H, 2·7; N, 21·5; Ni, 11·3%).

Dibromotribenzotetrazaporphin.—(a) *Preparation.* A solution of tribenzotetrazaporphin (57 mg.) in chlorobenzene (12 l.) was divided into 2-l. portions. Each was stirred and treated with bromine (0·5 c.c.), and 10 min. later was washed with 2N-sodium carbonate (2 × 200 c.c.) and with water (2 × 200 c.c.) and filtered through cotton wool. Concentration of the combined solutions to 25 c.c., and cooling, yielded *dibromotribenzotetrazaporphin* (60·6 mg., 79%), which, on extractive crystallisation from chlorobenzene, formed dark blue needles with a purple reflex (Found: C, 54·1; H, 2·7; N, 18·3; Br, 25·7. $C_{28}H_{14}N_8Br_2$ requires C, 54·0; H, 2·3; N, 18·0; Br, 25·7%).

(b) *Oxidative degradation.* A solution of the pigment (86·2 mg.) in concentrated sulphuric acid (4 c.c.) at 0° was treated rapidly with 0·01N-potassium dichromate (20 c.c.) and then kept at 70° for 5 min. Ferrous sulphate (0·5 g.) was added and the solution extracted with benzene for 48 hr. The extract was treated with charcoal, dried (Na_2SO_4), and evaporated, and the residue was taken up in ether, and the solution filtered and evaporated, but inorganic

[11] Brockmann and Schodder, *Ber.*, 1941, **74**, 73.
[12] B.P. 565,405/1944; Kaplan and Meller, *J. Gen. Chem.* (*U.S.S.R.*) (U.S. trans.), 1949, **19**, 507.

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contaminants had not been removed. Attempts to separate the mixture of imides by fractional sublimation, adsorption chromatography in chloroform on alumina, and partition chromatography between ether or ethyl acetate and water on silica gel were abortive. However, paper chromatography was successful.

Dibromomaleimide (5 mg.), phthalimide (5 mg.), 4-bromophthalimide (5 mg.), a 1 : 3 : 1 mixture of these three imides (10 mg.), and the degradation product (10 mg.) were dissolved separately in butanol (1-c.c. portions). The solutions (2 drops of each) were applied to a sheet (12 × 12 in.) of Whatman no. 1 filter paper to form a row of 5 spots near to the lower edge, and the paper was developed upwards with butanol saturated with aqueous ammonia (*d* 0·88), in a glass tank, until the solvent front had advanced 20—30 cm. (*ca.* 9 hr.). The paper was dried in the air for 4 hr., dipped in 1 : 1 acetone–ethanol, blotted, and when almost dry, exposed to chlorine gas (in a tank) for 10 min. The paper was dipped for 2 min. into a 1 : 1 mixture of saturated *o*-tolidine in 2% acetic acid and 0·05N-potassium iodide in 2% acetic acid. The paper was washed with 2% acetic acid, blotted, and dried in the air. The chromatogram appeared as blue spots, which faded to a permanent pale brown (cf. ref. 13). R_F values were :

Dibromomaleimide	0·25		
Phthalimide		0·56	
4-Bromophthalimide			0·70
1 : 3 : 1 Mixture of imides	0·26	0·54	0·71
Degradation product	0·26	0·53	

Dibromomaleimide.—Dunlap's method [4] was modified in that dibromomaleic anhydride [14] (1 g.) was fused with urea (0·35 g.) at 85—90° for 2 hr. (We found his original conditions led to decomposition and polymerisation.) Treatment of the cold, red-brown melt with water (100 c.c.) left dibromomaleimide (146 mg., 15%), m. p. 220° undepressed by a sample (m. p. 225—227°) obtained in 7% yield *via* the bromination of succinimide.[15] Ciamician and Silber [15] give m. p. 225°.

4-Bromophthalimide.—4-Nitrophthalimide [16] was reduced to 4-aminophthalimide.[17] A solution of the amine (5·4 g.) in concentrated sulphuric acid (15 c.c.) was cooled in an ice-salt mixture, and stirred with powdered sodium nitrite (2·6 g.). Subsequently, potassium bromide (13 g.) was added to the greenish solution (frothing), which was cooled again, and then copper powder (8 g.) was added in portions (frothing). After 15 min., the mixture was poured into ice-water (200 c.c.) (frothing), and the filtrate was extracted with benzene overnight. Concentration of the extract afforded 4-bromophthalimide (1·24 g.), m. p. 213—218°, which after recrystallisation from acetic acid had m. p. 229° (Found : N, 6·5. Calc. for $C_8H_4O_2NBr$: N, 6·2%). Waldmann's bromophthalimide [3] had m. p. 225—229°.

Monobenzotetrazaporphin.—Material from the mauve band in the kieselguhr chromatograms [1] and from the mother-liquors from the crystallisation of tribenzotetrazaporphin (above) was bulked. A solution in chlorobenzene (2 l.; 10 mg.) was run on to a column (4 × 90 cm.) of kieselguhr (acid-washed, British Drug Houses, Ltd.) and the chromatogram developed with chlorobenzene. Coloured zones separated, and were eluted, and the constituents identified, as follows : (1) Blue, eluted in *ca.* 30 l., $\lambda_{max.}$ 675, 594, 566, 349 mμ, tribenzotetrazaporphin. (2) Mauve, eluted in *ca.* 15 l., $\lambda_{max.}$ 641, 599, 589, 345 mμ, monobenzotetrazaporphin (Fig. 2). (3) Pale blue, eluted in *ca.* 3 l., $\lambda_{max.}$ (visible) 661, 641, 629, 599, 589, 565 mμ, unaffected by hydrochloric acid : a mixture of monobenzotetrazaporphin and a (? heavy)metal tribenzotetrazaporphin. (4) Green, eluted by 3 : 97 ethanol–chlorobenzene (1 l.), $\lambda_{max.}$ 622, 569, 340, 295 mμ, demetallated by cold hydrochloric acid [solution then had $\lambda_{max.}$ identical with fraction (2)], ? magnesium monobenzotetrazaporphin (see Fig. 2).

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Department of Chemistry, Imperial College of Science and Technology,
South Kensington, London, S.W.7. [*Received, January 16th*, 1957.]

[13] Rydon and Smith, *Nature*, 1952, **169**, 922; Reindel and Hoppe, *Chem. Ber.*, 1954, **87**, 1103.
[14] Diels and Reinbeck, *Ber.*, 1910, **43**, 1274.
[15] Ciamician and Silber, *Ber.*, 1884, **17**, 556.
[16] *Org. Synth.*, Coll. Vol. II, p. 459.
[17] Rodionov and Fedorova, *Bull. Soc. chim. France*, 1939, **6**, 478.

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482. *Carbonyl Complexes of Rhodium. Part II.* Complexes with Triaryl Phosphites.*

By Miss L. Vallarino.

The preparation and properties of complexes $[RhL_2(CO)Cl]$ and $[RhL_3Cl]$ (L = triaryl phosphite) are described. These compounds are monomers, non-electrolytes, and diamagnetic. The complexes $[RhL_2(CO)Cl]$ are similar to, but less stable than, the analogous compounds with triarylphosphines. On treatment with an excess of triaryl phosphite they give complexes of the type $[RhL_3Cl]$. The complexes $[RhL_2(CO)Cl]$ react with sodium thiocyanate, losing carbon monoxide and giving compounds $[Rh_2L_4(SCN)_2]$ which are diamagnetic, non-electrolytes, and have a binuclear structure with bridging thiocyanate groups.

The triaryl derivatives of tervalent phosphorus, arsenic, and antimony react (cf. Part I *) with tetracarbonyl-$\mu\mu'$-dichlorodirhodium thus:

$$[Rh_2(CO)_4Cl_2] + 4L \longrightarrow 2[RhL_2(CO)Cl] + 2CO$$
$$(L = Ar_3P, Ar_3As, \text{and } Ar_3Sb)$$

Triaryl phosphites used in this reaction gave two series of compounds: $[RhL_2(CO)Cl]$ and $[RhL_3Cl]$ where L = $(PhO)_3P$, $(p\text{-}C_6H_4Me\cdot O)_3P$, or $(p\text{-}C_6H_4Cl\cdot O)_3P$). The former, which are formally analogous to the products isolated with triphenylphosphine, can be prepared by using the stoicheiometric amount of triaryl phosphite, and the latter by using an excess of phosphite.

That triarylphosphines do not give compounds $[RhL_3Cl]$ even under very drastic conditions is in agreement with the previous observation that triaryl phosphites with metal carbonyls tend to give products poorer in carbon monoxide than those obtained by reaction with triarylphosphines.

The compounds of both series, $[RhL_2(CO)Cl]$ and $[RhL_3Cl]$, are non-electrolytes in nitrobenzene solution, monomeric, and diamagnetic. The complexes prepared, and their properties, are listed in the Table.

Triaryl phosphite complexes of rhodium(I).

Complex	Decomp. pt.	
$[Rh\{(C_6H_5\cdot O)_3P\}_2(CO)Cl]$	160—170°	Pale yellow needles
$[Rh\{(p\text{-}C_6H_4Me\cdot O)_3P\}_2(CO)Cl]$	170—176	Pale yellow needles
$[Rh\{(p\text{-}C_6H_4Cl\cdot O)_3P\}_2(CO)Cl]$	180—185	Yellow plates
$[Rh\{(C_6H_5\cdot O)_3P\}_3Cl]$	170—180	Yellow needles
$[Rh\{(p\text{-}C_6H_4Me\cdot O)_3P\}_3Cl]$	166—167	Yellow needles
$[Rh\{(p\text{-}C_6H_4Cl\cdot O)_3P\}_3Cl]$	183—186	Pale yellow needles
$[Rh\{(p\text{-}C_6H_4Me\cdot O)_3P\}_3(SCN)]$	150—170	Yellow prisms
$[Rh\{(p\text{-}C_6H_4Cl\cdot O)_3P\}_3(SCN)]$	158—160	Yellow prisms
$[Rh\{(p\text{-}C_6H_4Cl\cdot O)_3P\}_3I]$	135—136	Orange prisms
$[Rh_2\{(p\text{-}C_6H_4Me\cdot O)_3P\}_4(SCN)_2]$	150—175	Yellow prisms

Compounds $[RhL_3Cl]$ are stable to dilute aqueous acid and strong base, and to boiling concentrated hydrochloric acid. They do not possess reducing properties and are not attacked by strong reducing agents such as hypophosphorous acid in aqueous alcohol, hydrazine hydrate in ethanol, or metals (magnesium, zinc, and cadmium). They do not react with aromatic amines or pyridine, but are decomposed by aryl *iso*cyanides with formation of tetra*iso*cyanorhodium(I) salts.

The chlorine in the compounds $[RhL_3Cl]$ can be replaced by iodine or thiocyanate in acetone solution by means of sodium iodide or thiocyanate respectively. These derivatives are analogous to the corresponding chlorides, but the iodide is less stable. The solid does not alter on storage for several months, but its solutions, when exposed to the air, become brown within a few hours.

* Part I, 1957, 2287.

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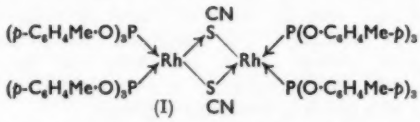
The complexes $[RhL_2(CO)Cl]$ behave analogously to the corresponding phosphine complexes, but are more reactive towards triaryl phosphites and sodium thiocyanate. With the former they lose carbon monoxide and give $[RhL_3Cl]$. They react with a suspension of sodium thiocyanate in acetone in the cold: carbon monoxide is liberated and, when $[Rh\{(p\text{-}C_6H_4Me\cdot O)_3P\}_2(CO)Cl]$ is used as a starting material, a yellow crystalline product can be isolated; this is a non-electrolyte in nitrobenzene solution and diamagnetic, has the composition $[Rh\{(p\text{-}C_6H_4Me\cdot O)_3P\}_2(SCN)]$, and must be formulated as a dimer with bridging thiocyanate groups (cf. I). Molecular-weight determinations are not



(I)

reliable because of the very low solubility of this product. The formulation is, however, supported by the infrared spectrum. It is known [2] that in the thiocyanato-complexes of platinum(II) terminal thiocyanate groups absorb in the region of 2100—2150 cm.$^{-1}$, while bridging thiocyanate groups absorb between 2150 and 2182 cm.$^{-1}$. Compound (I) has a strong absorption band at 2150 cm.$^{-1}$ while in the monomeric complex $[Rh\{(p\text{-}C_6H_4Me\cdot O)_3P\}_3(SCN)]$, in which the thiocyanate group is certainly terminal, does not absorb in this region but has a strong absorption band at 2092 cm.$^{-1}$.

The preceding three types of rhodium(I)–phosphite complex should have square planar configuration, and $[RhL_2(CO)Cl]$ should exist in *cis*- and *trans*-forms. It is probable that they have *trans*-configuration, in analogy with the similar derivatives of phosphines and arsines (Part I).

Experimental

Carbonylbis(triphenyl Phosphite)chlororhodium(I), $[Rh\{(Ph\cdot O)_3P\}_2(CO)Cl]$.—A solution of triphenyl phosphite (4 mmols.) in benzene (50 ml.) was added to a solution of tetracarbonyldichlorodirhodium (1 mmol.) in benzene (20 ml.). Carbon monoxide was evolved and the colour of the solution changed from orange to yellow. The solution was taken to dryness at 15 mm., giving a yellow oil which was washed with ethanol. This was treated in chloroform with charcoal, filtered, and diluted with ethanol. Crystals slowly separated. The *complex* was purified further by reprecipitation from chloroform with ethanol (Found: P, 8·0; Rh, 12·95%; *M*, cryoscopic in 2·3% benzene solution, 770. $C_{37}H_{30}O_7ClP_2Rh$ requires P, 7·9; Rh, 13·1%; *M*, 787). It is soluble in methylene chloride, chloroform, benzene, and nitrobenzene, moderately soluble in acetone and ethyl ether, insoluble in methanol, ethanol, and hexane. It is diamagnetic.

The following were prepared and purified analogously:

*Carbonylbis(tri-*p*-tolyl phosphite)chlororhodium*(I), $[Rh\{(p\text{-}C_6H_4Me\cdot O)_3P\}_2(CO)Cl]$ (Found: P, 6·4; Rh, 11·5%; *M*, cryoscopic in 2·2% benzene solution, 865. $C_{43}H_{42}O_7ClP_2Rh$ requires P, 7·1; Rh, 11·8%; *M*, 871), $\chi_m = -464 \times 10^{-6}$.

*Carbonylbis(tri-*p*-chlorophenyl phosphite)chlororhodium*(I), $[Rh\{(p\text{-}C_6H_4Cl\cdot O)_3P\}_2(CO)Cl]$ (Found: P, 6·4; Rh, 10·4; CO, 3·0%; *M*, cryoscopic in 2·4% benzene solution, 990. $C_{37}H_{24}O_7Cl_7P_2Rh$ requires P, 6·2; Rh, 10·4; CO, 2·8%; *M*, 994), $\chi_m = -474 \times 10^{-6}$.

*Attempted Reaction of Carbonylbis(tri-*p*-chlorophenyl Phosphite)chlororhodium with* p*-Toluidine and Pyridine.*—The complex (0·1 g.) in chloroform (10 ml.) and an excess of *p*-toluidine were refluxed for 10 min. The solution was cooled and on dilution with ethanol a crystalline product was obtained (0·075 g.) which did not contain nitrogen and evolved carbon monoxide on addition of aryl*iso*cyanides. It was identical with the starting material, as shown by its infrared spectrum.

The starting material was also recovered unchanged after being boiled with pyridine in chloroform and identified by its infrared spectrum.

*Reaction of Carbonylbis(tri-*p*-chlorophenyl Phosphite)chlororhodium with* p*-Tolyl* iso*Cyanide.*—*p*-Tolyl *iso*cyanide was added to the complex suspended in ethanol. Carbon monoxide was

[1] Malatesta and Sacco, *Ann. Chim.* (*Italy*), 1954, **44**, 134.
[2] Chatt and Duncanson, *Nature*, 1956, **178**, 997.

evolved and the starting material dissolved, giving a brown-red solution. On addition of sodium perchlorate in ethanol a violet crystalline product separated, which in boiling benzene gave yellow $[Rh(p\text{-}C_6H_4Me\cdot NC)_4]ClO_4$ (Found: N, 8·5; Rh, 15·2. Calc. for $C_{32}H_{28}O_4NClRh$: N, 8·3; Rh, 15·35%).

*Reaction of Carbonylbis(tri-*p*-tolyl Phosphite)chlororhodium with Sodium Thiocyanate.*—Solid sodium thiocyanate (0·15 g.) was added to the complex (0·4 g.) suspended in acetone (15 ml.); there was gas evolution and the solid changed in appearance. The mixture was boiled for 10 min. and then the solvent evaporated at 15 mm. The residual solid was extracted with chloroform; the solution was filtered and diluted with ethanol. Crystals separated at once, and were filtered off, washed with ethanol, and purified by reprecipitation with ethanol from a chloroform solution (yield 0·3 g.). They were *tetrakis(tri-*p*-tolyl phosphite)-μμ′-dithiocyanatodirhodium*, $[\{(p\text{-}C_6H_4Me\cdot O)_3P\}_4Rh_2(SCN)_2]$ [Found: C, 59·2; H, 5·1; N, 1·8%; *M*, cryoscopic in 0·66% benzene solution, 1400 (not very reliable because of low solubility). $C_{86}H_{84}O_{12}N_2S_2P_4Rh_2$ requires C, 59·65; H, 4·9; N, 1·6%; *M*, 1731]. It is appreciably less soluble than the other compounds described. It is diamagnetic. It does not evolve carbon monoxide when treated with aryl *iso*cyanides, even at 100°.

Tris(triphenyl Phosphite)chlororhodium(I), $[Rh\{(Ph\cdot O)_3P\}_3Cl]$.—Triphenyl phosphite (8 mmols.) was added to a solution of tetracarbonyldichlorodirhodium (1 mmol.) in benzene. The solution was evaporated to a small volume at 15 mm. and diluted with ethanol. The *complex* obtained was recrystallised from chloroform by addition of ethanol (yield 1·75 g.) (Found: P, 8·4; Rh, 9·55%; *M*, cryoscopic in 3·4% benzene solution, 1035. $C_{54}H_{45}O_9ClP_3Rh$ requires P, 8·7; Rh, 9·6%; *M*, 1069). It is slightly less soluble than its carbonyl analogue. It is diamagnetic.

The following were prepared and purified analogously:

*Tris(tri-*p*-tolyl phosphite)chlororhodium*(I), $[Rh\{(p\text{-}C_6H_4Me\cdot O)_3P\}_3Cl]$ (Found: P, 7·7; Rh, 8·7%; *M*, cryoscopic in 3·0% benzene solution, 1100. $C_{63}H_{63}O_9ClP_3Rh$ requires P, 7·8; Rh, 8·6%; *M*, 1195), $\chi_m = -746\cdot\times 10^{-6}$.

*Tris(tri-*p*-chlorophenyl phosphite)chlororhodium*(I), $[Rh\{(p\text{-}C_6H_4Cl\cdot O)_3P\}_3Cl]$ (Found: Cl, 25·95; P, 6·7; Rh, 7·5%; *M*, cryoscopic in 8% bromoform solution, 1410. $C_{54}H_{36}O_9Cl_{10}P_3Rh$ requires Cl, 25·7; P, 6·7; Rh, 7·5%; *M*, 1379), $\chi_m = -396 \times 10^{-6}$.

An attempted reaction of tris(tri-*p*-chlorophenyl phosphite)chlororhodium with *p*-toluidine, as described for the carbonyl compound, gave unchanged starting material (infrared spectrum).

*Tris(tri-*p*-tolyl Phosphite)thiocyanatorhodium*(I), $[Rh\{(p\text{-}C_6H_4Me\cdot O)_3P\}_3(SCN)]$.—The chloro-complex (0·4 g.) and sodium thiocyanate (0·3 g.) in acetone were refluxed for 15 min., then taken to dryness under reduced pressure, and the residual solid was extracted with chloroform. The solution was filtered and diluted with ethanol. A crystalline *product* was obtained (0·31 g.), which was purified as its chloro-analogue (Found: N, 1·3; S, 2·8%; *M*, cryoscopic in 1·2% benzene solution, 1233. $C_{64}H_{63}O_9NSP_3Rh$ requires N, 1·15; S, 2·6%; *M*, 1218). It is diamagnetic.

*Tris(tri-*p*-chlorophenyl Phosphite)thiocyanatorhodium*(I), $[Rh\{(p\text{-}C_6H_4Cl\cdot O)_3P\}_3(SCN)]$.—This *compound* was prepared and purified as its *p*-tolyl analogue (yield 0·5 g. from 0·6 g.) (Found: N, 1·15; S, 2·45%. $C_{55}H_{30}O_9NCl_9SP_3Rh$ requires N, 1·0; S, 2·3%). It is diamagnetic.

*Tris(tri-*p*-chlorophenyl Phosphite)iodorhodium*(I), $[Rh\{(p\text{-}C_6H_4Cl\cdot O)_3P\}_3I]$.—This complex, prepared and purified analogously to the corresponding thiocyanate (yield 0·2 g. from 0·3 g. of chloro-complex and 0·15 g. of sodium iodide) (Found: C, 43·8; H, 2·65%; *M*, cryoscopic in 1·6% benzene solution, 1410. $C_{54}H_{36}O_9Cl_9IP_3Rh$ requires C, 44·0; H, 2·5%; *M*, 1475), is diamagnetic.

Conductance Measurements.—None of the compounds described shows electric conductance in 10^{-3}m-nitrobenzene solution at 20°.

Infrared Spectra.—The compounds were finely ground and suspended in Vaseline. Their infrared spectra were taken with a Perkin-Elmer spectrophotometer (type 21), a rock-salt prism and cell being used. No compensation was made for the absorption of the Vaseline.

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483. *The Dipole Moments of Some Aromatic Nitro-compounds in relation to the Steric Inhibition of the Mesomeric Effect of the Nitro-group.*

By A. C. Littlejohn and J. W. Smith.

The dipole moments of some derivatives of nitrobenzene, *m*-dinitrobenzene, and 1 : 3 : 5-trinitrobenzene have been determined from measurements on benzene solutions. After inductive effects have been taken into account, the results, in conjunction with other data, indicate that an *ortho*-chlorine atom, -bromine atom, or -*tert.*-butyl group reduces considerably the effective group moment of a nitro-group. A methyl group has a much smaller effect. However, only when substituents occupy both positions *ortho* to the nitro-group, or when one substituent in such a position has also another substituent adjacent to it, is the group moment reduced almost to that of a nitro-group in a saturated aliphatic compound. It is shown that appreciable out-of-plane deflection of the groups in these compounds is improbable, and the results are interpreted in terms of slight in-plane deflection of the bonds between the substituents and the benzene nucleus together with a reduction in the effective moment of the nitro-group arising from steric inhibition of its mesomeric effect.

It has been shown [1,2] that the use of the classical laws of induction assists in interpreting the dipole moments of a number of monosubstituted diphenyls and 2 : 2′- and 3 : 3′-disubstituted diphenyls, the most self-consistent results being obtained when the effective centres of the dipoles of the substituents are assumed to lie near to their polarisable centres. An attempt has been made, therefore, to use this method to assist in interpreting the dipole moments of polysubstituted benzenes, especially those for which the values appear to be anomalous. These include molecules with large balanced dipoles, and nitro-compounds in which the mesomeric effects of the nitro-groups may be partially or completely inhibited through steric factors.

To augment the data available for comparison, the dipole moments of *m*-dinitrobenzene and of various derivatives of nitrobenzene, *m*-dinitrobenzene, and 1 : 3 : 5-trinitrobenzene have been determined from measurements on benzene solutions. The results are recorded in Table 1, where α, β, and γ are the limiting values of $d\varepsilon/dw$, dv/dw, and dn^2/dw, respectively, at zero concentration, and the other symbols have their usual significance. In calculating the dipole moment values it has been assumed that ${}_{\mu}P_2 = P_{2\infty} - [R_D]_2$. For trinitro- and tribromo-compounds, however, where atom polarisation may contribute appreciably to the value of $P_{2\infty}$ the moments have also been calculated by making further allowances for atom polarisation equal to the $P - [R_D]$ differences for 1 : 3 : 5-trinitrobenzene [3] (9·6 c.c.) and 1 : 3 : 5-tribromobenzene [4] (2·1 c.c.), respectively. The values of the dipole moments, in benzene solution, so deduced are shown in parentheses in Table 1 : they are regarded as the more probable values and are used in the subsequent discussion.

The measurements on *m*-dinitrobenzene, *p*-chloronitrobenzene, and *p*-bromonitrobenzene, repeated on account of the variations in the recorded values, agree closely with those of Le Fèvre and Le Fèvre [3] and of Tiganik.[4] Tiganik's results, when recalculated with modern values of the universal constants, lead to dipole moment values almost identical with ours.

It has been confirmed that the dipole moment of *m*-dinitrobenzene is appreciably smaller than that of nitrobenzene, although on simple vector theory the values should be equal. The dipole moments of the *m*-dihalogenobenzenes are also smaller than those of the corresponding monohalogenobenzenes. The classical laws of induction can be used to calculate the moment induced in each substituent by the presence of the other, and hence

[1] Littlejohn and Smith, *J.*, 1953, 2456.
[2] *Idem*, *J.*, 1954, 2552.
[3] Le Fèvre and Le Fèvre, *J.*, 1950, 1829.
[4] Tiganik, *Z. phys. Chem.*, 1931, **13**, *B*, 425.

to derive " theoretical " values of the moments of the disubstituted benzenes. For this purpose the dipoles have been assumed to be effectively located at the polarisable centres of the substituent groups : for the nitro-group this is 1·95 Å from the nucleus of the carbon atom to which it is linked, whilst for the halogen substituents it is at the nucleus of the

TABLE 1. *Summary of polarisation data for benzene solutions.*

	100α	$-10^3\beta$	$10^3\gamma$	$P_{2\infty}$ (c.c.)	$[R_D]_2$ (c.c.)	μ (D)	Previous values (D)
m-Dinitrobenzene	957	468	132	336·7	37·6	3·83	3·81,[5] 3·78,[4] 3·81,[4] * 3·96,[6] 3·86[3]
2 : 4-Dinitrodiphenyl	859	426	254	446·9	63·3	4·34	
2 : 4 : 6-Trinitrodiphenyl	118	484	267	121·1	70·7	1·57 (1·41)	
p-Chloronitrobenzene	475	419	143	174·8	37·8	2·59	2·36,[7] 2·34,[8] 2·57,[4] 2·59,[4] * 3·12[3]
p-Bromonitrobenzene	402	566	179	187·7	41·2	2·68	2·45,[8] 2·65,[4] 2·67[4] *
1-Chloro-2 : 4-dinitrobenzene	607	520	169	262·5	42·5	3·28	3·29,[10] 3·00,[11] 3·24[3]
1-Bromo-2 : 4-dinitrobenzene	522	625	173	280·4	45·8	3·39	3·1[11]
1 : 3 : 5-Tribromo-2-nitrobenzene	312	729	155	255·8	54·5	3·14 (3·12)	
1 : 3 : 5-Tribromo-2 : 4-dinitrobenzene	276	742	155	258·8	59·8	3·12 (3·10)	
1-*tert.*-Butyl-2 : 4-dinitrobenzene	1000	335	79	475·8	56·6	4·53	

* Recalculated.

halogen atom. By using the same polarisability values as in the previous work,[2] it is found that such mutual induction can account for only a small fraction of the differences observed between the moments of mono- and *m*-di-substituted benzenes (Table 2). Further, as the distances between the substituents are relatively large in these compounds, the calculated effect of mutual induction is comparatively insensitive to the exact locations assumed for the dipoles.

TABLE 2. *Parameters assumed for substituent groups and the observed and calculated dipole moments of* m-*disubstituted benzenes.*

Group X	Polarisability (10^{-25} c.c.)	Distance from ring carbon atom of dipole and polarisable centre	Dipole moments (D) PhX	m-$C_6H_4X_2$ obs.	m-$C_6H_4X_2$ calc.
Nitro	2·24	1·95	4·01	3·83 †	3·98
Chloro	1·91	1·69	1·58[1]	1·49 *	1·57
Bromo	3·05	1·88	1·56[1]	1·47 *	1·55
Iodo	5·07	2·00	1·40[1]	1·28 *	1·39

* Recalc. from Tiganik's results.[4] † Present work.

The effect is still more pronounced in *ortho*-disubstituted benzenes, for which, on simple vector theory, the dipole moments should be 1·732 times the values for the corresponding mono-substituted benzenes. Although for these compounds the calculated inductive effects of the substituents upon one another depend rather critically upon the location assumed for the dipole, such effects can account for only about one-third of the apparent reduction in the group moments. Mutual repulsion of the groups may be responsible in part for the reduction in the moments of the *ortho*-compounds, but in *meta*-disubstituted benzenes it is much too feeble to cause an increase of about $2\frac{1}{2}°$ in the angle between the dipoles which would be necessary to account for the observed values of the dipole moments. It also seems improbable that the results are due to solvent effects, as these are likely to be relatively smaller for the disubstituted than for the monosubstituted benzenes. A reduction in the mesomeric effect of each group in the presence of the other

[5] Williams and Schwingel, *J. Amer. Chem. Soc.*, 1928, **50**, 362.
[6] Higasi, *Bull. Inst. Phys. Chem. Res. Japan*, 1941, **20**, 218.
[7] Walden and Werner, *Z. phys. Chem.*, 1929, **2**, *B*, 10.
[8] Lütgert, *ibid.*, 1931, **14**, *B*, 350.
[9] Jagielski and Weslowski, *Bull. Acad. polon. Sci.*, 1935, *A*, 260.
[10] Hassel and Naeshagen, *Z. phys. Chem.*, 1931, **13**, *B*, 79.
[11] Lütgert, *Z. phys. Chem.*, 1932, **17**, *B*, 460.

would account for the lower moment of *m*-dinitrobenzene than of nitrobenzene, but would be expected to cause the moments of the *m*-dihalogenobenzenes to be greater than those of the corresponding monohalogenobenzenes. The most probable explanation, therefore, is that although the total displacement of the electrons of the ring brought about by the inductive effect of the substituents is greater in the *meta*-disubstituted benzenes than in the monosubstituted benzenes, the effect attributable to each substituent is less in the former than in the latter. Hence in calculating "theoretical" values of the dipole moments of derivatives of *m*-dinitro- or *m*-dihalogeno-benzenes it seems most logical to assume the effective group moments to be equal to the moment of this disubstituted compound.

This has been done when deriving the calculated moments given in Table 3. Here the figures shown under μ (calc.) (*a*) are the values obtained by vector addition, assuming no distortion of the valency angles and without correction for inductive effects of one group upon another. The figures under μ (calc.) (*b*), on the other hand, include corrections for these inductive effects: in deriving these it has been assumed that the polarisabilities

TABLE 3. *Observed and calculated dipole moments of nitro-compounds.*

	μ (obs.) (D)	μ (calc.) (D) (*a*) neglecting induction	μ (calc.) (D) (*b*) with allowance for induction	Effective moment of *o*-nitro-group (D)
4-Nitrodiphenyl	4·36	4·01	4·18	—
2 : 4-Dinitrodiphenyl	4·33	3·83	4·13	—
2 : 4 : 6-Trinitrodiphenyl	1·57 (1·41)	0·0	1·32	—
p-Nitrotoluene	4·44 [4]	4·38	4·42	—
o-Nitrotoluene	3·72 [4]	3·83	3·86	3·87
2 : 4 : 6-Trinitrotoluene	1·37 (1·19) [3]	0·37	0·75	3·33
Nitromesitylene	3·67 [3]	4·01	4·10	3·58
p-tert.-Butylnitrobenzene	4·64 [12]	4·54	4·65	—
1-*tert.*-Butyl-2 : 4-dinitrobenzene	4·53	4·09	4·70	3·54
p-Chloronitrobenzene	2·57	2·43	2·45	—
o-Chloronitrobenzene	4·36 [4]	4·99	4·86	3·57
1-Chloro-2 : 4-dinitrobenzene	3·32	3·33	3·39	3·65
2-Chloro-1 : 3 : 5-trinitrobenzene	1·13 (0·90) [3]	1·53	1·42	3·30
2 : 4-Dichloro-1-nitrobenzene	2·66 [12]	3·51	3·38	3·62
2 : 5-Dichloro-1-nitrobenzene	3·48 [3]	4·01	3·99	3·50
1 : 3-Dichloro-5-nitrobenzene	2·66 [12]	2·52	2·54	—
p-Bromonitrobenzene	2·65	2·45	2·49	—
o-Bromonitrobenzene	4·23 [4]	4·97	4·86	3·47
1-Bromo-2 : 4-dinitrobenzene	3·39	3·34	3·46	3·63
1 : 3 : 5-Tribromo-2-nitrobenzene	3·14 (3·12)	4·01	3·81	3·31
1 : 3 : 5-Tribromo-2 : 4-dinitrobenzene	3·12 (3·10)	3·83	3·79	3·31

of the methyl and the *tert.*-butyl group are 1·91 and 7·42 c.c., respectively, that their group moments are −0·37 and −0·53 D, respectively, and that their polarisable centres are located 1·55 Å and 2·07 Å, respectively, from the nucleus of the ring carbon atom to which they are bonded. For other groups the data shown in Table 2 were used. In calculating the theoretical moments of derivatives of 1 : 3 : 5-trinitrobenzene or 1 : 3 : 5-tribromobenzene the effective group moments of the nitro-group and bromine atom have been taken as equal to the dipole moments of the *m*-disubstituted compounds, although a slightly lower figure might be more correct. As these arise only in calculating the inductive effects in other substituents, however, the error arising from this cause cannot be very great.

In addition to the compounds the dipole moments of which have been determined in the present work, Table 3 includes a number of related compounds for which comparable data are available. Where necessary the original experimental results have been reassessed, using modern methods of extrapolation of the data and modern values of the universal constants.

On the simple vector addition theory the dipole moment of 2 : 4 : 6-trinitrodiphenyl

[12] Le Fèvre, Le Fèvre, and Robertson, *J.*, 1935, 480.
[13] Thomson, *J.*, 1944, 404.

should be zero. The greatest contribution to the substantial moment which is observed must come from the inductive effect, and hence it is satisfactory that, in spite of the somewhat arbitrary assumptions which have to be made, especially regarding the dielectric constant of the intervening medium between the polarisable groups and the polar groups, and the locations of the dipoles, the calculated moment is relatively near to the observed value, the difference being actually less than for 4-nitrodiphenyl. The moments of *p*-nitrotoluene and *p-tert.*-butylnitrobenzene are within experimental error of the calculated values, but those of *p*-chloro- and *p*-bromo-nitrobenzene exceed the calculated values by 0·12 and 0·16 D, respectively. Such differences have usually been ascribed to the mutual enhancement of the mesomeric effects of *op*- and *m*-directing groups when they occupy positions *para* to one another. It is significant, however, that the dipole moment of 1 : 3-dichloro-5-nitrobenzene also exceeds the calculated value by 0·12 D, although in this compound the mesomeric effects of the nitro-group and of the chlorine atoms cannot mutually enhance one another. It seems possible, therefore, that the increase in the moments of these compounds over the calculated values may be due rather to the withdrawal of electron density from the ring through the strong inductive and mesomeric effects of the nitro-group. This will cause the displacement of the ring electrons by the inductive effects of the halogen atoms to be much less than in the halogenobenzenes, so that the effective " group " moments of the chlorine and bromine atoms are reduced to about 1·46 and 1·40 D, respectively. In support of this argument it may be added that, in spite of the fact that the mesomeric effect of the fluorine atom is greater than that of other halogen atoms, the observed moment of *p*-fluoronitrobenzene [14] (2·64 D) is only 0·11 D in excess of the calculated value.

So far as the other compounds listed in Table 3 are concerned, however, there is another factor which must come into play. The mesomeric contribution to the dipole moment of nitrobenzene depends upon the overlap of the π-orbitals of the nitro-group with the π-orbitals of the benzene ring. This in turn demands that the three atoms of the nitro-group can come into or near to the plane of the ring. When such coplanarity is inhibited through steric causes, as in nitromesitylene and nitrodurene,[15] the overlap is decreased and hence the effective moment of the nitro-group is reduced. In the limit, if such overlap were prevented completely, the moment of the nitro-group would be expected to be reduced to the value which it has in saturated aliphatic compounds, *i.e.*, about 3·25 D. Some such restriction must be expected in all compounds which contain a nitro-group in a position *ortho* to other substituents. The observed moments of the various nitro-compounds have therefore been used in calculating the values of the group moments of the nitro-groups in positions *ortho* to other substituents. In these calculations it has been assumed that any other nitro-groups present in the molecule retain an effective value of 3·83 D, as in *m*-dinitrobenzene, and that the effective group moments of chlorine and bromine are 1·46 and 1·40 D, respectively. The values so deduced are shown in the last column of Table 3.

In spite of the evidence obtained by Bastiansen and Hassel [16] from electron-diffraction measurements that the C–Cl bonds in such compounds as *o*-dichlorobenzene and hexachlorobenzene are deflected at least 12° out of the plane of the ring, dielectric polarisation evidence is against such a state of affairs for 1 : 3 : 5-trihalogeno-2 : 4 : 6-trinitrobenzene and the trihalogeno- and trinitro-mesitylenes. Tiganik's values [4] for the $P_{2\infty} - [R_D]_2$ differences for *sym*-trichloro-, -tribromo-, and -trinitro-benzene and mesitylene are 2·1, 2·1, 10·7, and 0·5 c.c., respectively. These are of the order to be expected for the atom polarisations of molecules with balanced dipoles of the magnitudes present in the respective compounds. For 1 : 3 : 5-trichloro- and 1 : 3 : 5-tribromo-2 : 4 : 6-trinitrobenzene, however, the corresponding differences are only 9·0 and 9·5 c.c., respectively. As would be

[14] Leonard and Sutton, *J. Amer. Chem. Soc.*, 1948, **70**, 1565.
[15] Kofod, Sutton, de Jong, Verkade, and Wepster, *Rec. Trav. chim.*, 1952, **71**, 521.
[16] Bastiansen and Hassel, *Acta Chem. Scand.*, 1947, **1**, 489.

expected if the in-plane vibrations are more restricted than in the *sym*-trisubstituted benzenes, these values are appreciably less than the sums of the differences for the parent compounds. If the C–halogen and C–N bonds were each deflected 12° alternately on each side of the plane of the ring, as visualised by Bastiansen and Hassel for hexachlorobenzene, the trihalogenotrinitrobenzenes should have dipole moments of the order of 1·5 D, corresponding with an orientation polarisation at 20° of about 47 c.c. In these compounds there is a chance that the relative deflections of the chlorine and nitrogen atoms may be such that all moment contributions cancel out, but such could not be the case for mesitylene derivatives. The $P_{2\infty} - [R_D]_2$ differences for trichloro-, tribromo-, and trinitro-mesitylene are 3·2, 2·8, and 13·6 c.c., respectively. These values are very little greater than the sums of the corresponding differences for the parent compounds, whereas if the groups were deflected 12° out of the plane of the ring, so that all three methyl groups were on one side and the other substituents on the opposite side, orientation polarisations of 31 c.c. for the trihalogenomesitylenes and 140 c.c. for trinitromesitylene would be expected. Even if the molecules were distributed between various structures with out-of-plane deflections of the groups such that adjacent groups are not always on opposite sides of the plane of the ring, the mean orientation polarisation would still be expected to be quite appreciable. The evidence suggests, therefore, that when nitro-groups and halogen atoms or methyl groups alternate round the ring the out-of-plane deflection of the C–N and C–X bonds can only be very slight. Similar conclusions were reached by Kofod, Kumar, and Sutton [17] with regard to the groups in trichloromesitylene. It seems most logical to assume, therefore, that in all the compounds discussed here any bond deflection occurs in the plane of the ring and not at right angles to it.

An in-plane deflection of the groups in positions *ortho* to one another will modify the dipole moment of the molecule, and hence will lead to errors in the calculated value of the moment of the nitro-group. The sense of the error, however, depends on the nature of the substituents, and hence each compound must be considered separately. Thus an increase in the angle between the C–N and C–Me bond axes in *o*-nitrotoluene above the value of 60° assumed in deriving the calculated moments given in Table 3 would increase the dipole moment of the molecule: hence the figure of 3·87 D derived for the effective moment of the nitro-group is a maximum value. For *o*-chloro- and *o*-bromo-nitrobenzene, on the other hand, an increase in the angle between the axes of the C–N and C–halogen bonds would decrease the dipole moment of the molecule, so the calculated values of the nitro-group moment (3·57 and 3·47 D, respectively) are minimum figures. Amonst the trisubstituted benzenes studied, in-plane deflection of the groups *ortho* to one another would decrease the dipole moments of 2 : 4- and 2 : 5-dichloro-1-nitrobenzene, so the calculculated nitro-group moments (3·62 and 3·50 D, respectively) are minimum values. Similar deflection, however, would have only a slight effect on the moments of 2 : 4-dinitro-1-halogenobenzenes, so the moments of the *o*-nitro-groups in these molecules are probably very near to the calculated values (3·65 and 3·63 D, respectively). For 1-*tert.*-butyl-2 : 4-dinitrobenzene a deflection would increase the dipole moment, and the calculated group moment must be interpreted as a maximum value.

Comparison of the figures for the various compounds studied suggests, therefore, that the effective moment of a nitro-group with one substituent in a position *ortho* to it varies with the nature of this group; for Bu^t, Br, Cl, and Me it is about 3·5, 3·63, 3·65, and 3·8 D, respectively. On this evidence the steric effects of these groups upon the mesomerism of the nitro-group follow the expected order, but, excepting perhaps for the *tert.*-butyl group, one *ortho*-group is insufficient to reduce the effective moment of a nitro-group to the value it shows in a saturated aliphatic compound.

In the 2 : 4 : 6-trisubstituted nitrobenzenes the nitro-group will not undergo in-plane displacement, so it is to be expected that the C–Me bonds in nitromesitylene, for instance, may undergo greater deflection than the C–Me bond in *o*-nitrotoluene, but the angle

[17] Kofod, Kumar, and Sutton, *J.*, 1951, 1790.

between the C–N and C–Me bond axes will be less than in the latter compound. Hence the steric obstruction to coplanarity of the nitro-group with the ring may be expected to be greater in trisubstituted nitrobenzenes than in *o*-monosubstituted nitrobenzene. Similar conditions should prevail in the *sym*-trinitro-compounds, where only the nitro-groups *ortho* to the other substituent can undergo permanent in-plane deflection. Again the angle between the C–N and C–X bond axes will be less than in the corresponding *o*-nitro-compound, and since it seems probable that a nitro-group may tend to suffer less in-plane deflection than other groups, the steric obstruction to mesomerism of the *o*-nitro-groups in 2 : 4 : 6-trinitrotoluene would be expected to be greater than in nitromesitylene.

These conclusions are supported by the calculated values of the effective moments of the *o*-nitro-groups in these compounds. A small increase in the angle between the C–Me and C–N bond axes will increase the moment of nitromesitylene very slightly but that of 2 : 4 : 6-trinitrotoluene much more, so, bearing in mind the directions of the dipoles in the two compounds, it can be inferred that the calculated nitro-group moments (3·58 and 3·33 D) are maximum and minimum values, respectively, although the value for nitromesitylene is probably nearly correct. By analogous arguments the group moments calculated from the dipole moments of 2-chloro-1 : 3 : 5-trinitrobenzene, 1 : 3 : 5-tribromo-2-nitrobenzene, and 1 : 3 : 5-tribromo-2 : 4-dinitrobenzene, 3·30, 3·31, and 3·31 D respectively, are all minimum values. The fact that they are almost equal could be accounted for by assuming that the angle of deflection of the C–N bonds in the trinitro-compound is about two-fifths of the deflection of the C–Br bonds in the tribromo-compounds, but it seems most likely that the effective moments of the *o*-nitro-groups in these compounds are not much more than 3·30 D, which is little above the nitro-group moment in a saturated aliphatic compound (about 3·25 D). Further, since it is improbable that the deflection of the C–N bonds in 2 : 4 : 6-trinitrotoluene is greater than in 1-bromo-2 : 4 : 6-trinitrobenzene, the effective moments of the *o*-nitro-groups in 2 : 4 : 6-trinitrotoluene must be lower than that of the nitro-group in nitromesitylene, as is to be expected if the mesomeric effect of the nitro-groups is more restricted sterically in the former than in the latter.

The evidence suggests, therefore, that in 2-chloro-1 : 3 : 5-trinitrobenzene, 1 : 3 : 5-tribromo-2-nitrobenzene, and 1 : 3 : 5-tribromo-2 : 4-dinitrobenzene the mesomeric effects of the nitro-groups *ortho* to a halogen atom are almost wholly suppressed. The effect may be less fully suppressed, however, in 2 : 4 : 6-trinitrotoluene, and is only partially suppressed in nitromesitylene. As for the trisubstituted nitrobenzenes, halogen atoms in positions *ortho* to the nitro-group are more effective in inhibiting its mesomeric effect than are methyl groups, but in each case the influence of the substituent group is more pronounced in the trinitro-compounds than in trisubstituted nitrobenzenes. This is attributable to a " buttressing " action, resulting in a reduced in-plane deflection of groups which have other groups in the two positions *ortho* to them. In this connection it may be pertinent that, although the dipole moment of nitrodurene might be expected to be equal to or, if inductive effects are taken into account, slightly greater than, that of nitromesitylene, the experimental value [15] (3·62 D) seems to be significantly lower. This may be attributable to a decreased deflection of the methyl groups *ortho* to the nitro-group, and the consequent decrease in the mesomeric effect of the latter, through the presence of the methyl groups in the *meta*-positions.

Experimental

Materials.—Benzene was purified, dried as previously described,[1] and redistilled under anhydrous conditions immediately before use.

Commercial samples of pure *m*-dinitrobenzene, *p*-chloronitrobenzene, *p*-bromonitrobenzene, 1-chloro-2 : 4-dinitrobenzene, and 1-bromo-2 : 4-dinitrobenzene were recrystallised from alcohol and had m. p. 91°, 83°, 127°, 51°, and 75°, respectively. 2 : 4-Dinitrodiphenyl and 2 : 4 : 6-trinitrodiphenyl, prepared by Ullmann's method [18] from iodobenzene and 1-chloro-2 : 4-dinitrobenzene or 2-chloro-1 : 3 : 5-trinitrobenzene, and recrystallised from alcohol and light petroleum,

[18] Gull and Turner, *J.*, 1929, 496.

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respectively, had m. p. 111° and 131°, respectively. 1 : 3 : 5-Tribromo-2-nitrobenzene was prepared by Loudon's method [19] from 1 : 3 : 5-tribromobenzene, and crystallised repeatedly from chloroform : it had m. p. 125°. 1 : 3 : 5-Tribromo-2 : 4-dinitrobenzene and 1-*tert.*-butyl-2 : 4-dinitrobenzene, kindly lent by Professor E. E. Turner and Dr. M. S. Lesslie, respectively, were recrystallised from alcohol and had m. p. 192° and 62°, respectively.

Methods.—Dielectric constants, specific volumes, and refractive indices were measured at 25° by the method used previously, excepting that the dielectric constant of pure benzene was assumed to be 2·2741.[20] The results are shown in Table 4. The $P_{2\infty}$ and $[R_D]_2$ values were derived both from the parameters α, β, and γ and from the specific polarisations of the individual solutions, the results for the two methods being in satisfactory agreement.

TABLE 4. *Polarisation data for benzene solutions at 25°*

100*w*	ε	*v*	n_D	100*w*	ε	*v*	n_D
	m-*Dinitrobenzene*				1-*Chloro*-2 : 4-*dinitrobenzene*		
0·0000	2·2741	1·14462	1·4980	0·0000	2·2741	1·14462	1·4980
1·1541	2·3851	1·13921	1·4985	1·2290	2·3494	1·13823	1·4988
1·6037	2·4291	1·13711	1·4987	1·7889	2·3839	1·13531	1·4990
2·2839	2·4956	1·13396	1·4990	2·3200	2·4173	1·13256	1·4993
2·6689	2·5337	1·13213	1·4992	2·6489	2·4381	1·13089	1·4994
3·1343	2·5793	1·12996	1·4994	3·5601	2·4954	1·12610	1·5000
4·1034	2·6761	1·12542	1·4998	4·4756	2·5546	1·12135	1·5005
	2 : 4-*Dinitrodiphenyl*				1-*Bromo*-2 : 4-*dinitrobenzene*		
0·0000	2·2741	1·14462	1·4890	0·0000	2·2741	1·14460	1·4980
0·4234	2·3104	1·14280	1·4983	1·5173	2·3541	1·13562	1·4988
0·8419	2·3469	1·14103	1·4987	2·7904	2·4232	1·12715	1·4995
1·2726	2·3846	1·13922	1·4991	3·4429	2·4590	1·12313	1·4999
1·6832	2·4208	1·13746	1·4994	4·1361	2·4974	1·11872	1·5005
2·0686	2·4550	1·13581	1·4998	5·6251	2·5811	1·10949	1·5012
2·4544	2·4890	1·13418	1·5001				
	2 : 4 : 6-*Trinitrodiphenyl*				1 : 3 : 5-*Tribromo*-2-*nitrobenzene*		
0·0000	2·2741	1·14462	1·4980	0·0000	2·2741	1·14463	1·4980
0·7696	2·2832	1·14094	1·4986	1·0851	2·3082	1·13674	1·4985
1·3026	2·2896	1·13830	1·4992	1·7179	2·3286	1·13206	1·4989
1·8233	2·2957	1·13582	1·4996	2·1283	2·3418	1·12922	1·4991
2·1980	2·3000	1·13399	1·5000	2·7229	2·3611	1·12473	1·4994
2·7388	2·3064	1·13138	1·5004	3·4192	2·3842	1·11969	1·4998
2·9797	2·3092	1·13025	1·5007	3·6486	2·3916	1·11800	1·4999
	p-*Chloronitrobenzene*				1 : 3 : 5-*Tribromo*-2 : 4-*dinitrobenzene*		
0·0000	2·2741	1·14460	1·4980	0·0000	2·2741	1·14460	1·4980
0·5268	2·2992	1·14239	1·4982	1·3596	2·3119	1·13448	1·4987
1·1977	2·3315	1·13958	1·4984	1·9237	2·3265	1·13033	1·4989
2·1048	2·3754	1·13578	1·4989	2·9748	2·3586	1·12254	1·4995
2·8501	2·4129	1·13266	1·4993	5·4337	2·4307	1·10434	1·5008
3·6325	2·4507	1·12931	1·4996	7·5147	2·4956	1·08881	1·5019
4·5610	2·4970	1·12539	1·5001	8·5021	2·5264	1·08162	1·5024
5·2193	2·5301	1·12279	1·5005				
	p-*Bromonitrobenzene*				1-tert.-*Butyl*-2 : 4-*dinitrobenzene*		
0·0000	2·2741	1·14460	1·4980	0·0000	2·2741	1·14458	1·4979
0·6691	2·3013	1·14081	1·4984	0·7682	2·3516	1·14206	1·4981
1·7010	2·3434	1·13497	1·4990	1·5262	2·4284	1·13944	1·4983
2·7694	2·3876	1·12891	1·4996	2·4297	2·5217	1·13641	1·4985
3·7271	2·4275	1·12350	1·5002	3·1200	2·5935	1·13418	1·4987
4·8622	2·4751	1·11709	1·5009	4·2742	2·7150	1·13022	1·4991
5·8573	2·5214	1·11102	1·5016				

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BEDFORD COLLEGE, REGENT'S PARK, LONDON, N.W.1. [*Received, January 30th,* 1957.]

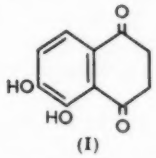
[19] Loudon, *J.*, 1940, 1525.
[20] Hartshorn, Parry, and Essen, *Proc. Phys. Soc.*, 1955, **68**, *B*, 422.

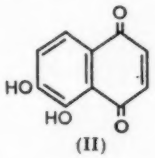
484. *Quinones. Part VI.* Some New Polyhydroxynaphthaquinones.*

By J. F. Garden and R. H. Thomson.

5 : 6- and 5 : 7-Dihydroxy- and 2 : 3 : 5- and 2 : 3 : 6-trihydroxy-1 : 4-naphthaquinone have been synthesised. Some new properties of hydroxynaphthaquinones are described.

We have shown [1] that the compound regarded by Dimroth and Roos [2] as 5 : 6-dihydroxy-1 : 4-naphthaquinone is, in fact, 5-amino-6-hydroxy-1 : 4-naphthaquinone. They obtained it by nitration of 6-hydroxy-1 : 4-naphthaquinone followed by reduction to a trihydroxynaphthylamine and oxidation with ferric chloride. Acetylation of the intermediate trihydroxynaphthylamine gives a tetra-acetyl derivative identical with that obtained by reductive acetylation of the quinone. Authentic 5 : 6-dihydroxy-1 : 4-naphthaquinone (*o*-naphthazarin) (II) has now been prepared from 3 : 5 : 6-trihydroxy-1 : 4-naphthaquinone by reduction with acid stannous chloride.[3] The diketone (I), isolated initially,


(I)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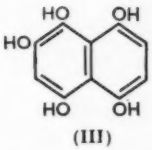
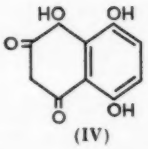

(III)


(IV)

was converted into (II) by aeration in alkaline solution. In an effort to improve the overall yield of 3 : 5 : 6-trihydroxy-1 : 4-naphthaquinone [3] the intermediate 5-chloro-7 : 8-dimethoxytetralone was condensed with *p*-nitrosodimethylaniline before hydrogenolysis, but removal of chlorine from the resulting 5-chloro-2-hydroxy-7 : 8-dimethoxy-1 : 4-naphthaquinone was difficult. 5 : 6-Dihydroxy-1 : 4-naphthaquinone closely resembles naphthazarin in its behaviour in alkaline solution, the cornflower-blue colour remaining unchanged after several days whereas Dimroth and Roos's compound is unstable and soon becomes red therein. *o*-Naphthazarin also forms a blue solution in aqueous sodium hydrogen carbonate, as does 5-amino-6-hydroxy-1 : 4-naphthaquinone. As 6-hydroxy- and 5 : 7-dihydroxy-1 : 4-naphthaquinone are also soluble in this reagent hydroxyl groups at positions 6 and 7 are evidently strongly acidic (Dimroth and Roos prepared a monopyridine salt from their compound) and are readily distinguished from the chelated hydroxyl groups at positions 5 and 8 which confer solubility only in sodium carbonate. In this respect hydroxynaphthaquinones differ from analogous anthraquinones; the α-hydroxy-derivatives in that series are soluble in sodium carbonate and very rarely (in certain polyhydroxy-derivatives, *e.g.*, 1 : 3 : 6 : 8-tetrahydroxyanthraquinone) in sodium hydrogen carbonate solution.

As 5 : 7-dihydroxy-1 : 4-naphthaquinone was required for our work on spinochrome N, this has also been synthesised. In principle it should be possible to derive this from 2(or 3) : 5 : 7-trihydroxy-1 : 4-naphthaquinone by reduction with stannous chloride but the synthesis of both intermediates is somewhat tedious.[4] In the case of the 2 : 5 : 7-isomer (flaviolin) the main difficulty lies in the cyclisation of γ-(2 : 4-dimethoxyphenyl)-butyric acid to the corresponding tetralone, the yield being very low. Where similar difficulty (*i.e.*, cyclisation *meta* to two *ortho*/*para*-directing groups) has been encountered in the formation of anthraquinones from *o*-benzoylbenzoic acids, bromination of the

* Part V, *J.*, 1955, 1089.

[1] Garden and Thomson, *Chem. and Ind.*, 1954, 1146.
[2] Dimroth and Roos, *Annalen*, 1927, **456**, 177.
[3] Bruce and Thomson, *J.*, 1952, 2759; 1954, 1428.
[4] Davies, King, and Roberts, *J.*, 1955, 2782.

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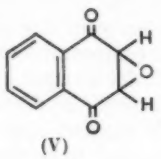
" unreactive " ring has, on occasion, greatly assisted the ring closure.[5] However this device did not succeed in the present instance, the yield of bromodimethoxytetralone being very poor. This route to 5 : 7-dihydroxy-1 : 4-naphthaquinone was not pursued. The most direct method, *i.e.*, condensation of maleic anhydride with resorcinol or 4-chlororesorcinol (cf. ref. 6) also failed, presumably for the same reason. Another approach to flaviolin, namely, alkaline oxidation of 1 : 3 : 6 : 8-tetrahydroxynaphthalene, could not be carried through as attempts to obtain the latter by alkali fusion of chromotropic acid invariably disrupted the molecule and only 2 : 4-dihydroxybenzoic acid could be isolated (cf. ref. 7). Finally the desired compound was obtained by reduction of naphthapurpurin with alkaline sodium stannite. Probably the quinol (III) formed initially reacts in the tautomeric form (IV) from which the " benzyl " hydroxyl group is removed. The resultant tetrahydroxynaphthalene was taken into ether and oxidised directly with silver oxide. For convenience naphthapurpurin triacetate was used as starting material; this is readily prepared by oxidation of naphthazarin to 1 : 4 : 5 : 8-naphthadiquinone followed by Thiele acetylation of the crude material.[8] This type of reduction has been effected in the anthraquinone series (*e.g.*, purpurin ⟶ xanthopurpurin [9]) where much milder conditions suffice. The new quinone is unstable in the presence of acids, becoming green, but acetylation in the presence of sodium acetate afforded a diacetate which showed typical 1 : 4-naphthaquinone ultraviolet absorption. With the synthesis of 5 : 7-dihydroxy-1 : 4-naphthaquinone all the possible dihydroxy-1 : 4-naphthaquinones are now known.

Most of the polyhydroxynaphthaquinones occurring in sea urchins (in which we are interested) contain two hydroxyl groups in the quinone ring. 2 : 3-Dihydroxy-1 : 4-naphthaquinone itself has been obtained by several methods,[10] most of which are of limited value. Weygand's procedure,[11] an unusual benzoin condensation of phthalaldehyde with glyoxal in the presence of cyanide ion, is of general application but is limited by the inaccessibility of substituted phthalaldehydes. Shchukina *et al.*[12] have



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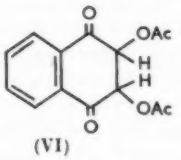
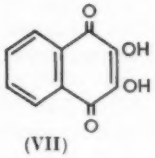


(VI)



(VII)

converted 1 : 4-naphthaquinone into its 2 : 3-dihydroxy-derivative *via* the epoxide (V) and the glycol diacetate (VI), which on aeration in alkaline solution is smoothly converted into the quinone (VII). This is a more flexible method and enables two hydroxyl groups to be introduced into any *Bz*-substituted naphthaquinone provided the epoxides can be obtained. The latter are prepared under alkaline conditions which have not been successfully applied to *Bz*-hydroxylated naphthaquinones whilst acid reagents (including trifluoroperoxyacetic acid) are ineffective. It is therefore necessary to protect such hydroxyl groups, which has hitherto been difficult, especially for strongly chelated *peri*-hydroxyl groups. Only three such quinones (naphthazarin,[13] flaviolin,[14] and cordeauxiaquinone [15]) have been

[6] Jacobson and Adams, *J. Amer. Chem. Soc.*, 1924, **46**, 1312.
[7] Cooke and Dowd, *Austral. J. Chem.*, 1953, **6**, 53.
[8] Meyer and Hartman, *Ber.*, 1905, **38**, 3945.
[9] Zahn and Ochwat, *Annalen*, 1928, **462**, 72; Fieser and Dunn, *J. Amer. Chem. Soc.*, 1937, **59**, 1019.
[10] G.P. 212,697; Hill and Richter, *J.*, 1936, 1714.
[11] " Encyclopaedia of Organic Chemistry," Vol. XII, B, p. 3178. Elsevier, Amsterdam, 1952.
[12] Weygand, *Ber.*, 1942, **75**, 625.
[13] Shchukina, Vinogradova, and Shemyakin, *J. Gen. Chem.* (*U.S.S.R.*), 1951, **21**, 1661.
[14] Brass, Pfluger, and Honsberg, *Ber.*, 1936, **69**, 87.
[15] Astill and Roberts, *J.*, 1953, 3302.
[16] Lister, Eugster, and Karrer, *Helv. Chim. Acta*, 1955, **38**, 215.

successfully methylated and previous attempts to methylate juglone,[16] the simplest example, failed. We now find that methyl iodide–silver oxide in chloroform solution (but not in dimethylformamide [17]) is a convenient methylating reagent for this purpose and 5-hydroxy-, 6-hydroxy-, and 5 : 8-dihydroxy-1 : 4-naphthaquinone have been smoothly converted into their methyl ethers. The yield of naphthazarin dimethyl ether is only moderate but the procedure is more convenient than that of Brass *et al.*[13] who used methyl toluene-*p*-sulphonate. By use of the Russian method, the 2 : 3-dihydroxy-derivatives of these ethers were prepared from which the 2 : 3 : 5-(new) and 2 : 3 : 6-trihydroxy-1 : 4-naphthaquinones were obtained by demethylation. 5 : 8-Dimethoxy-1 : 4-naphthaquinone 2 : 3-epoxide was obtained earlier [18] but was regarded as the 2-hydroxy-derivative on account of its solubility in aqueous sodium hydroxide. However the epoxide is genuine (there is no OH band in its infrared spectrum in chloroform solution) but readily hydrolyses in alkaline solution to form 2-hydroxy-5 : 8-dimethoxy-1 : 4-naphthaquinone which was also obtained by methylation of naphthapurpurin and subsequent hydrolysis. Simple 2-hydroxy-1 : 4-naphthaquinones form red solutions in aqueous sodium hydroxide, but we have noticed that the colour usually shifts towards orange-yellow when a *peri*-methoxyl group is introduced. The effect is more striking when two such groups are present: 2-hydroxy-5 : 8-dimethoxy-1 : 4-naphthaquinone gives an amber solution in alkali, and 2 : 3-dihydroxy-5 : 8-dimethoxy-1 : 4-naphthaquinone a red colour, whereas 2 : 3-dihydroxy-1 : 4-naphthaquinone itself forms a blue alkaline solution.

Certain substituents attached to a quinone ring, *e.g.*, halogen or alkylthio-groups, are readily replaced by hydroxyl on treatment with alkali, but a second hydroxyl group cannot be introduced adjacent to the first in this way. Acid hydrolysis should be more effective. This was examined briefly but the results were discouraging and anomalous. By using sulphuric acid it was possible to replace one substituent in 2 : 3-dichloronaphthazarin and in 2 : 3-dibenzylthio-1 : 4-naphthaquinone; the latter with hydrobromic acid unexpectedly yielded a little 2-hydroxy-1 : 4-naphthaquinone. Hydrolysis of 2-phenylthio-1 : 4-naphthaquinone with hydrobromic acid proceeded normally but no definite products could be isolated after acid hydrolysis of 2-acetoxy-3-*p*-tolylthio-1 : 4-naphthaquinone.

Experimental

5-Amino-6-hydroxy-1 : 4-naphthaquinone.—6-Hydroxy-5-nitro-1 : 4-naphthaquinone was prepared by Dimroth and Roos's method.[8] It crystallised from glacial acetic acid in yellow *needles*, m. p. 285—289° (decomp.) (54%) (Found: C, 54·6; H, 2·4; N, 6·4. $C_{10}H_5O_5N$ requires C, 54·8; H, 2·3; N, 6·4%). The nitroquinone (5·5 g.) was added in portions to a stirred solution of stannous chloride (55 g.) in concentrated hydrochloric acid (110 ml.) at 60°. After 5 min. the solution became colourless and, on cooling, 5-amino-1 : 4 : 6-trihydroxynaphthalene hydrochloride separated. This was dissolved in water (1050 ml.) and oxidised by the slow addition of ferric chloride (12 g.) in water (350 ml.). The dark red solution was set aside and the precipitate collected next day. 5-Amino-6-hydroxy-1 : 4-naphthaquinone crystallised from a large volume of water in dark red, almost black, crystals with a metallic lustre, m. p. 196—200° (48%). They formed a cornflower-blue solution in aqueous sodium hydrogen carbonate. Reductive acetylation yielded a tetra-acetyl derivative forming plates, m. p. 201—202° (from ethanol), identical with the product obtained by acetylation of 5-amino-1 : 4 : 6-trihydroxynaphthalene hydrochloride. The aminohydroxyquinone (0·3 g.) in acetic anhydride (5 ml.) was heated under reflux for 5 min., allowed to cool slowly, and set aside for 5 days. The *diacetyl derivative* was collected and recrystallised from benzene in red needles, m. p. 187° (decomp.) (Found: C, 61·8; H, 4·2; N, 5·3. $C_{14}H_{11}O_5N$ requires C, 61·55; H, 4·05; N, 5·1%). A mixture of the aminohydroxyquinone (0·3 g.), benzoyl chloride (0·3 ml.), and pyridine (3 ml.) was stirred for 15 min., red needles of 5-amino-6-benzoyloxy-1 : 4-naphthaquinone being deposited. These were collected and rearrangement was effected by warming

[16] Fierz-David, Blangey, and Krannichfeldt, *ibid.*, 1947, **30**, 827.
[17] Kuhn, Trischmann, and Löw, *Angew. Chem.*, 1955, **67**, 32.
[18] Bruce and Thomson, *J.*, 1955, 1089.

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them in glacial acetic acid (4 ml.) at 35°. On cooling, *5-benzamido-6-hydroxy-1 : 4-naphthaquinone* separated and was recrystallised from the same solvent, forming red needles, m. p. 165—170° (decomp.) (Found : C, 69·35; H, 4·0; N, 4·7. $C_{17}H_{11}O_4N$ requires C, 69·6; H, 3·8; N, 4·8%).

1 : 2 : 3 : 4-Tetrahydro-5 : 6-dihydroxy-1 : 4-dioxonaphthalene.—3 : 5 : 6-Trihydroxy-1 : 4-naphthaquinone (0·6 g.) was added to a hot solution of stannous chloride (3 g.) in 5N-hydrochloric acid (130 ml.) and boiled under reflux for 30 min. The solution was filtered and repeatedly extracted with chloroform whilst still warm. More hydrochloric acid (20 ml.; 6N) was added to the aqueous phase which was then refluxed for 30 min. and again extracted with chloroform. The process was repeated once more. Evaporation of the combined, dried ($CaCl_2$) extracts left a residue which crystallised from light petroleum (b. p. 100—120°) in pale fawn needles, m. p. 186° (decomp.) (27%) (Found : C, 62·35; H, 4·2. $C_{10}H_8O_4$ requires C, 62·45; H, 4·2%). The *diketone* formed a green solution in aqueous sodium hydroxide which became cornflower-blue on being kept. Treatment with cold acetic anhydride containing a drop of concentrated sulphuric acid afforded *1 : 4 : 5 : 6-tetra-acetoxynaphthalene* in needles, m. p. 178° (from aqueous acetic acid) (Found : C, 60·1; H, 4·3; Ac, 43·0. $C_{18}H_{16}O_8$ requires C, 60·0; H, 4·5; Ac, 47·5%).

5 : 6-Dihydroxy-1 : 4-naphthaquinone.—A brisk current of air was passed through a solution of the above diketone (0·5 g.) in 2N-aqueous sodium hydroxide (10 ml.) for 10 min. After filtration, the blue solution was acidified with hydrochloric acid, extracted with chloroform, and dried ($CaCl_2$). Removal of the solvent under reduced pressure left the *quinone* which separated from light petroleum (b. p. 100—120°) in red needles, m. p. 180—183° (decomp.) (66%) (Found : C, 63·1; H, 3·35. $C_{10}H_6O_4$ requires C, 63·1; H, 3·2%). Light absorption : $\lambda_{max.}$ (in EtOH) at 226, 263, and 461 mμ (log ε 4·15, 4·01, and 3·51 respectively), $\nu_{C:O}$ (in $CHCl_3$) 1666 (m) and 1644 (s) $cm.^{-1}$. *o*-Naphthazarin forms an intensely red solution in concentrated sulphuric acid and a red solution in pyridine which becomes deep blue on dilution with water. It gives a green ferric reaction and a deep blue precipitate with methanolic lead acetate. Acetylation with acetic anhydride, perchloric acid being used as catalyst, afforded yellow needles, m. p. 138—140°, but consistent analytical figures could not be obtained. Reductive acetylation gave the tetra-acetate, m. p. 178°, described above.

8-Chloro-3-hydroxy-5 : 6-dimethoxy-1 : 4-naphthaquinone.—10% Aqueous sodium hydroxide (3 ml.) was added to a solution of 5-chloro-1 : 2 : 3 : 4-tetrahydro-7 : 8-dimethoxy-1-oxonaphthalene (1·5 g.) and *p*-nitrosodimethylaniline (2·5 g.) in alcohol (100 ml.). After 4 days the violet precipitate (1·3 g.) was collected, washed with a little cold methanol, and dried. This dianil was then heated under reflux in a solution of concentrated sulphuric acid (6 ml.) and water (100 ml.) for 1 hr. The *hydroxy-quinone* was precipitated and was collected on cooling. It was combined with an additional amount obtained by chloroform extraction of the filtrate and purified by dissolution in dilute aqueous sodium hydrogen carbonate (charcoal). Acidification afforded golden needles which sublimed at 125°/0·02 mm. in yellow needles, m. p. 209° (26·1%) (Found : C, 53·4; H, 3·4; Cl, 12·9. $C_{12}H_9O_5Cl$ requires C, 53·6; H, 3·4; Cl, 13·3%). Light absorption : $\lambda_{max.}$ (in EtOH) 362 and 446—450 mμ (log ε 3·61 and 3·39 respectively). The *acetate* crystallised from glacial acetic acid in yellow needles, m. p. 187° (Found : C, 53·9; H, 3·7; Cl, 10·9. $C_{14}H_{11}O_6Cl$ requires C, 54·1; H, 3·6; Cl, 11·3%).

Naphthapurpurin Triacetate (cf. ref. 8).—Lead tetra-acetate (12·5 g.) was added gradually to a suspension of finely divided naphthazarin (5 g.) in glacial acetic acid (70 ml.) until the red colour had become yellow-brown. The dark purple diquinone was collected, washed with light petroleum, and added in portions to a stirred mixture of acetic anhydride (25 ml.) and concentrated sulphuric acid (1 ml.). The temperature rose to 40°. After 2 hr. the mixture was poured on ice, and the light orange precipitate crystallised from alcohol (charcoal) in orange-brown needles, m. p. 160° (3 g.). This material was sufficiently pure for reduction.

5 : 7-Dihydroxy-1 : 4-naphthaquinone.—A solution of sodium stannite was prepared by mixing warm solutions of stannous chloride (2·5 g.) in concentrated hydrochloric acid (5 ml.), and sodium hydroxide (7·5 g.) in water (15 ml.). After cooling and addition of a little Celite, the mixture was filtered and added to naphthapurpurin triacetate (0·5 g.). The alkaline solution was boiled under reflux for 5 hr., added to iced concentrated hydrochloric acid (25 ml.) and rapidly extracted with ether. The ether layer was shaken with saturated brine (containing a little sodium dithionite) and then filtered through anhydrous magnesium sulphate on to silver oxide (3 g.) mixed with a little of the desiccant. After the suspension had been shaken for

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30 min. it was filtered and evaporated. The residual *quinone* crystallised from toluene in orange needles, decomp. 165—170° (30%) (Found: C, 63·1; H, 3·05. $C_{10}H_6O_4$ requires C, 63·1; H, 3·2%). Light absorption: $\lambda_{max.}$ (in EtOH) 265 and 431 mμ (log ε 4·12 and 3·63 respectively), $\nu_{C=O}$ (in $CHCl_3$) 1675 (m) and 1642 (s) cm.$^{-1}$. The quinone gave a violet-red colour in aqueous sodium hydrogen carbonate and a green solution in concentrated sulphuric acid. Stirring in the cold with acetic anhydride and anhydrous sodium acetate afforded a *diacetate*, golden-yellow plates, m. p. 126—127° (decomp.) (Found: C, 61·7; H, 3·9. $C_{14}H_{10}O_6$ requires C, 61·3; H, 3·7%). Light absorption: $\lambda_{max.}$ (in EtOH) 233 and 342 mμ (log ε 4·5 and 3·6 respectively). Stirring the acetylation mixture in the cold with zinc dust yielded 1 : 4 : 5 : 7-*tetra-acetoxynaphthalene* which separated from ethyl acetate–light petroleum (b. p. 100—120°) in needles, m. p. 181° (Found: C, 60·3; H, 4·5. $C_{18}H_{16}O_8$ requires C, 60·0; H, 4·5%).

2 : 3 : 5-*Trihydroxy*-1 : 4-*naphthaquinone*.—A suspension of juglone (5 g.) in chloroform (125 ml.) was shaken vigorously with silver oxide (10 g.) and methyl iodide (7·5 ml.) for 1 hr. Two further additions of silver oxide (5 g.) and methyl iodide (4 ml.) were made at intervals of 1 hr. and shaking was continued until a test portion of the chloroform solution no longer gave a violet colour with aqueous sodium hydroxide. The mixture was filtered and the residue extracted with warm chloroform. Evaporation of the combined filtrates left juglone methyl ether which crystallised from methanol in orange needles, m. p. 187° (92%). To a solution of this quinone (5 g.) in alcohol (250 ml.) at 45° was added 30% hydrogen peroxide (20 ml.) and 30% aqueous sodium carbonate (17 ml.). Heat was evolved and the yellow colour faded. After being shaken at 45° for 5 min., the mixture was cooled and diluted with water (200 ml.), and kept at 0° overnight. The precipitate was collected, and further material was obtained by repeated extraction of the filtrate with ether. 5-*Methoxy*-1 : 4-*naphthaquinone* 2 : 3-*epoxide* separated from methanol in needles, m. p. 109° (57%) (Found: C, 64·8; H, 4·1. $C_{11}H_8O_4$ requires C, 64·7; H, 4·0%). The oxide (2 g.) in acetic anhydride (15 ml.) containing concentrated sulphuric acid (0·9 ml.) was stirred at room temperature for 10 min., with occasional cooling in ice, after which a solid mass separated. The product was collected, and washed with ether containing a little alcohol and with water. 2 : 3-*Diacetoxy*-1 : 2 : 3 : 4-*tetrahydro*-5-*methoxy*-1 : 4-*dioxonaphthalene* crystallised from methanol in needles, m. p. 185° (decomp.) (80%) (Found: C, 58·4; H, 4·8. $C_{15}H_{14}O_7$ requires C, 58·8; H, 4·6%). Hydrolysis and oxidation of the diacetate (0·5 g.) was effected by passing a brisk stream of air through its solution in aqueous sodium hydroxide (15 ml., 10%). After 10 min. the blue solution was filtered and acidified with dilute sulphuric acid. The precipitated 2 : 3-*dihydroxy*-5-*methoxy*-1 : 4-*naphthaquinone* formed red crystals, m. p. 229° (decomp.) (from glacial acetic acid) (70%) (Found: C, 59·9; H, 3·8. $C_{11}H_8O_5$ requires C, 60·0; H, 3·7%). Light absorption: $\lambda_{max.}$ (in EtOH) 382·5 and 540 mμ (log ε 3·46 and 3·23 respectively). The *diacetate* formed yellow needles, m. p. 201° (from benzene) (Found: C, 59·1; H, 3·9. $C_{15}H_{12}O_7$ requires C, 59·2; H, 3·95%). The dihydroxymethoxyquinone (0·8 g.) was demethylated by addition to a stirred melt of anhydrous aluminium chloride (24 g.) and sodium chloride (4·8 g.) at 140°. The temperature was quickly raised to 180—190° and maintained for 2 min. After cooling, the mixture was decomposed with 18% hydrochloric acid (360 ml.). The precipitated quinone was filtered off and a little more was obtained by chloroform extraction of the filtrate. 2 : 3 : 5-*Trihydroxy*-1 : 4-*naphthaquinone* crystallised from light petroleum (b. p. 100—120°) in red needles, m. p. 234° (decomp.) (45%) (Found: C, 58·1; H, 3·25. $C_{10}H_6O_5$ requires C, 58·2; H, 3·0%). Light absorption $\lambda_{max.}$ (in EtOH), 397 and 567 mμ (log ε 3·56 and 3·42 respectively). The *triacetate* crystallised from light petroleum (b. p. 100—120°) in yellow needles, m. p. 140° (Found: C, 57·7; H, 3·7. $C_{16}H_{12}O_8$ requires C, 57·8; H, 3·65%).

2 : 3 : 6-*Trihydroxy*-1 : 4-*naphthaquinone*.—6-Hydroxy-1 : 4-naphthaquinone (5 g.) was methylated by shaking it vigorously in chloroform (125 ml.) for 1 hr. with silver oxide (20 g.) and methyl iodide (15 ml.). The product formed yellow needles, m. p. 136° (from light petroleum) (80%), and was converted, as described above, into 6-*methoxy*-1 : 4-*naphthaquinone* 2 : 3-*epoxide* which crystallised from methanol in prisms, m. p. 109° (77%) (Found: C, 64·5; H, 3·8. $C_{11}H_8O_4$ requires C, 64·7; H, 4·0%). Acetylation as before yielded 2 : 3-*diacetoxy*-1 : 2 : 3 : 4-*tetrahydro*-6-*methoxy*-1 : 4-*dioxonaphthalene* in rosettes, m. p. 192° (from methanol) (75%) (Found: C, 58·6; H, 5·0. $C_{15}H_{14}O_7$ requires C, 58·8; H, 4·6%). Aeration in alkaline solution then yielded 2 : 3-*dihydroxy*-6-*methoxy*-1 : 4-*naphthaquinone* which crystallised from glacial acetic acid in red needles, m. p. 214—217° (decomp.) (60%) (Found: C, 60·0; H, 3·9. $C_{11}H_8O_5$ requires C, 60·0; H, 3·7%). The *diacetate* formed yellow needles, m. p. 169° (from

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light petroleum) (Found : C, 59·4; H, 4·1. $C_{15}H_{12}O_7$ requires C, 59·2; H, 3·95%). Demethylation of the dihydroxymethoxyquinone with aluminium chloride–sodium chloride yielded 2 : 3 : 6-trihydroxy-1 : 4-naphthaquinone which was sublimed at 175°/0·03 mm. and then crystallised from light petroleum (b. p. 100—120°), forming red needles, m. p. 300—305° (decomp.) (50%) (Weygand *et al.*[19] give m. p. 300°).

3-*Hydroxy*-6-*methoxy*-1 : 4-*naphthaquinone*.—A mixture of 6-methoxy-1 : 4-naphthaquinone 2 : 3-epoxide (3·3 g.), acetic anhydride (17 ml.) and concentrated sulphuric acid (1·5 ml.) was stirred for 15 min. at room temperature without external cooling. The solid product was collected, washed well with water, and dissolved in N-sodium hydroxide (60 ml.). The solution was stirred for 10 min. and acidified with sulphuric acid. The precipitate separated from glacial acetic acid as red crystals (1·8 g.) of indefinite m. p. which were chromatographed in chloroform on a column of alumina. Two bands appeared. Elution of the lower band with chloroform gave a quinone separating from glacial acetic acid in golden needles, m. p. 214° (decomp.) (1·1 g.) (Found : C, 64·7; H, 3·9. Calc. for $C_{11}H_8O_4$: C, 64·7; H, 3·95%). (Fieser *et al.*[20] give m. p. 220—222° for 3-hydroxy-6-methoxy-1 : 4-naphthaquinone; the 2-hydroxy-isomer [21] has m. p. 197—200°.) The *acetate* formed yellow needles, m. p. 123° (from methanol) (Found : C, 63·3; H, 4·2. $C_{13}H_{10}O_5$ requires C, 63·4; H, 4·1%). Elution of the upper band on the column with chloroform–glacial acetic acid yielded 2 : 3-dihydroxy-6-methoxy-1 : 4-naphthaquinone, m. p. 214—217° (0·5 g.).

2 : 3-*Dihydroxy*-5 : 8-*dimethoxy*-1 : 4-*naphthaquinone*.—A stirred solution of sublimed naphthazarin (2 g.) in chloroform (70 ml.) was heated under reflux on a water-bath for 8 hr. with freshly prepared silver oxide (5 g.) and methyl iodide (4 ml.). Four further additions of silver oxide (5 g.) and methyl iodide (4 ml.) were made at intervals of 3 hr. Silver compounds were then removed by filtration and the procedure repeated until a test portion of the chloroform solution gave no colour when shaken with aqueous sodium hydroxide. After filtration, the chloroform was passed through a column of alumina and evaporated. The residual naphthazarin dimethyl ether crystallised from light petroleum (b. p. 100—120°) as orange needles, m. p. 155° (31%). It was converted into the *oxide* as before, yielding yellow needles, m. p. 195° (from light petroleum) (60%) (Found : C, 61·45; H, 4·15. $C_{12}H_{10}O_5$ requires C, 61·5; H, 4·3%). A mixture of the oxide (0·87 g.), acetic anhydride (9 ml.), and concentrated sulphuric acid (0·8 ml.) was set aside for 24 hr. The solution was then poured into ice-water (50 ml.), and the precipitate collected, washed with a little cold methanol, and dried. Recrystallisation from methanol afforded 2 : 3-*diacetoxy*-1 : 2 : 3 : 4-*tetrahydro*-5 : 8-*dimethoxy*-1 : 4-*dioxonaphthalene* as needles, m. p. 182° (38%) (Found : C, 57·3; H, 5·0. $C_{16}H_{16}O_8$ requires C, 57·15; H, 4·8%). A solution of this compound (0·4 g.) in 10% alcoholic potassium hydroxide (8 ml.) was aerated for 10 min., poured into water (30 ml.), and acidified with dilute sulphuric acid. Evaporation of the dried (Na_2SO_4) ethereal extract of this solution left 2 : 3-*dihydroxy*-5 : 8-*dimethoxy*-1 : 4-*naphthaquinone* which crystallised from benzene in red crystals, m. p. 211—213° (decomp.) (Found : C, 57·35; H, 3·95. $C_{12}H_{10}O_6$ requires C, 57·6; H, 4·0%). The quinone gave a red solution in aqueous sodium hydroxide and in concentrated sulphuric acid. The *diacetate* crystallised from light petroleum (b. p. 80—90°) as yellow needles, m. p. 127° (Found : C, 57·7; H, 4·25. $C_{16}H_{14}O_8$ requires C, 57·5; H, 4·2%).

2-*Hydroxy*-5 : 8-*dimethoxy*-1 : 4-*naphthaquinone*.—(*a*) A solution of 5 : 8-dimethoxy-1 : 4-naphthaquinone 2 : 3-epoxide (0·35 g.) in N-sodium hydroxide (10 ml.) was kept at 30—35° for 5 min., filtered, and acidified with dilute sulphuric acid. The *product* was isolated by chloroform-extraction and crystallised from light petroleum (b. p. 100—120°) in orange needles, m. p. 200° (decomp.) (57%) (Found : C, 61·8; H, 4·3. $C_{12}H_{10}O_5$ requires C, 61·5; H, 4·35%). Light absorption : $\lambda_{max.}$ (in EtOH) 421 mμ (log ε 3·78). (*b*) Naphthapurpurin was methylated as described for naphthazarin. The crude trimethyl ether (0·5 g.) (it was difficult to purify) was dissolved in N-sodium hydroxide (15 ml.) by warming at 60° for a few minutes, and acidified. The precipitate obtained was sublimed at 135°/0·03 mm. and then crystallised from light petroleum, forming orange needles, m. p. and mixed m. p. 198—200° (decomp.).

2-*Chloro*-3-*hydroxynaphthazarin*.—To a solution of 2 : 3-dichloronaphthazarin (0·2 g.) in concentrated sulphuric acid (3 ml.), water (3 ml.) was added. The suspension was heated gently under reflux for 30 min., cooled, diluted with water, and extracted with ether. The

[19] Weygand, Vogelbach, and Zimmermann, *Ber.*, 1947, **80**, 391.
[20] Fieser and Brown, *J. Amer. Chem. Soc.*, 1949, **71**, 3615.
[21] Buu-Hoï and Cagniant, *Compt. rend.*, 1942, **214**, 87.

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ether solution was then extracted with 5% aqueous sodium hydrogen carbonate, from which *2-chloro-3-hydroxynaphthazarin* was precipitated on acidification. It formed red crystals, m. p. 183—187° (subl. and decomp.) (from light petroleum) (65%) (Found: C, 50·1; H, 2·15; Cl, 14·5. $C_{10}H_5O_4Cl$ requires C, 49·9; H, 2·1; Cl, 14·7%).

2-Benzylthio-3-hydroxy-1 : 4-naphthaquinone.—To a solution of 2 : 3-dibenzylthio-1 : 4-naphthaquinone (0·5 g.) in glacial acetic acid (15 ml.), 1 : 1 v/v sulphuric acid (3 ml.) was added. The red solution was heated under reflux for 3 hr., cooled, poured into water, and extracted with ether. The extract was washed with aqueous sodium carbonate (5%) from which the *hydroxyquinone* was precipitated by acidification. It crystallised from light petroleum (b. p. 80—90°) in red needles, m. p. 152° (0·21 g.) (Found: C, 68·8; H, 4·1; S, 10·4. $C_{17}H_{12}O_3S$ requires C, 68·9; H, 4·1; S, 10·8%). The *acetate* formed yellow needles, m. p. 138° (from light petroleum) (Found: C, 67·2; H, 4·4. $C_{19}H_{14}O_4S$ requires C, 67·4; H, 4·2%). Evaporation of the ether solution left starting material (0·15 g.). Under the same conditions hydrolysis with phosphoric acid–acetic acid gave the same result (lower yield) but the dibenzylthioquinone was unaffected by hydrochloric acid–acetic acid. Hydrolysis of the starting quinone (0·5 g.) in refluxing glacial acetic acid (4 ml.) containing 48% hydrobromic acid (3·1 ml.) gave, after 2 hr., a crude product which sublimed at 125°/0·03 mm. in orange crystals, m. p. 190° (70 mg.). These formed an acetate, m. p. and mixed m. p. with 2-acetoxy-1 : 4-naphthaquinone, 128°.

Hydrolysis of 2-Phenylthio-1 : 4-naphthaquinone.—A suspension of the quinone (0·5 g.) in glacial acetic acid (3 ml.) containing 48% hydrobromic acid (3 ml.) was refluxed for 2 hr., cooled, poured into water, and extracted with ether. After being washed with aqueous sodium carbonate, the ether solution was dried and evaporated. The residue was sublimed at 55°/0·01 mm. and then crystallised from aqueous methanol in plates, m. p. 60°, identical with diphenyl disulphide. Acidification of the alkaline extract yielded a product which was sublimed at 125°/0·02 mm., to give orange crystals, m. p. and mixed m. p. with 2-hydroxy-1 : 4-naphthaquinone, 188—190° (40 mg.).

2-Acetoxy-3-p-tolylthio-1 : 4-naphthaquinone.—Toluene-ω-thiol (0·35 g.) was added to a suspension of 2-acetoxy-1 : 4-naphthaquinone (0·56 g.) in ethanol (12 ml.). The mixture was gently warmed to effect complete dissolution and left overnight. A quinol separated and recrystallised from light petroleum (b. p. 80—90°) in needles, m. p. 158° (0·46 g.). This was dissolved in ethanol (5 ml.) and poured into a stirred solution of ferric chloride (10 ml., 70%). The resultant *quinone* was collected and crystallised from light petroleum (b. p. 80—90°) in yellow needles, m. p. 105° (0·32 g.) (Found: C, 67·4; H, 4·1; S, 8·5. $C_{19}H_{14}O_4S$ requires C, 67·4; H, 4·2; S, 9·4%). The products of acid hydrolysis could not be purified.

γ-(5-Bromo-2 : 4-dimethoxyphenyl)butyric Acid.—Bromine (1·1 mol.) was added to a stirred solution of γ-(2 : 4-dimethoxyphenyl)butyric acid (5 g.) in glacial acetic acid (15 ml.) at 10—12°. The mixture was left overnight at room temperature, refluxed for 3 min., cooled, and poured into water. The *product* was collected and crystallised from light petroleum (b. p. 80—90°) in needles, m. p. 107° (80%) (Found: C, 47·5; H, 5·0; Br, 26·4. $C_{12}H_{15}O_4Br$ requires C, 47·6; H, 5·05; Br, 26·6%).

8-Bromo-5 : 7-dimethoxy-1-tetralone.—The above acid (4·4 g.) was added to polyphosphoric acid (44 g.) at 165°. After 5 minutes' stirring, the mixture was cooled and poured into water. The ketone, isolated with ether, distilled at 140° (bath)/0·3 mm. (0·28 g.) and formed a *2 : 4-dinitrophenylhydrazone* which separated from acetic acid in orange needles, m. p. 205° (Found: C, 46·7; H, 3·8; N, 12·4. $C_{18}H_{17}O_6N_4Br$ requires C, 46·4; H, 3·6; N, 12·0%).

Alkali Fusion of Chromotropic Acid.—A mixture of chromotropic acid (sodium salt, 15 g.), potassium hydroxide (75 g.), and water (1·5 ml.) was heated at 290° for 15 min. The cooled melt was dissolved in water, acidified, and extracted with ether, and this extract in turn extracted with aqueous sodium hydrogen carbonate. Acidification of the alkaline solution afforded 2 : 4-dihydroxybenzoic acid, m. p. and mixed m. p. 210° (1·3 g.).

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485. *The Enzymic Synthesis and Degradation of Starch. Part XXIII.* Structural Requirements of D-Enzyme with Respect to Acceptors.*

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The capacities have been tested of nearly fifty sugars, sugar derivatives, and related compounds to act as acceptors of glycosyl radicals transferred from maltodextrins by the agency of potato D-enzyme. Acceptor activity shows a large measure of specificity. The most effective is D-glucose; only nine other substances showed appreciable activity.

It is shown by the use of methyl α-D-glucopyranoside as acceptor, that it is the $C_{(4)}$-hydroxyl group of the acceptor which receives the transferred glycosyl radical. This reaction has been used for the preparation, pure for the first time, of methyl α-maltoside, α-maltotrioside, and α-maltotetraoside.

In Part XX [1] we reported the preparation and properties of potato D-enzyme, which catalyses disproportionating reactions between maltodextrins by the simultaneous scission and synthesis of α-1 : 4-linkages. For example, a maltosyl radical can be transferred from one maltotriose molecule to another, giving glucose and maltopentaose. This reaction seems to be freely reversible since it was possible to incorporate [^{14}C]glucose into maltodextrins by incubation with D-enzyme and maltopentaose. The participation of glucose in the reaction can also be recognised by the observation of iodine-staining power. Maltopentaose and higher dextrins are disproportionated to chain products which are sufficiently long to form red iodine complexes; [1] the addition of glucose to such a digest in equilibrium causes the staining-power to disappear, presumably because the longer chains are shortened by transfer of segment to glucose. Similarly, when amylopectin is incubated with D-enzyme in the presence of glucose the staining power diminishes by a much greater amount than it does in its absence. Other substances exhibit this property, *e.g.* methyl α-glucoside, mannose, and xylose, presumably because of similarities between their structures and that of glucose. In an attempt to elucidate the mechanism of D-enzyme action, the activities of 47 sugars, glycosides, and sugar alcohols were examined as acceptors in the D-enzyme catalysed transfer. The method of testing was by iodine-staining after the substance had been added to an equilibriated D-enzyme digest of maltodextrins.

Table 1. *D-enzyme disproportionation. Activities of some carbohydrates as acceptors.*

Compounds with acceptor activity: (D-glucose = 100, equimolar basis):
Methyl α-D-glucoside (37), methyl β-D-glucoside (12), D-mannose (13), L-sorbose (10), methyl α-L-sorboside (5), D-xylose (10), maltose (11), sucrose (6), leucrose (34), αα-trehalose (10).

Compounds with no acceptor activity:
(*a*) Isomaltose, maltulose, melezitose; α-D-glucose 1-phosphate.
(*b*) Methyl 2 : 6-di-*O*-methyl-β-D-glucoside; cellobiose, gentiobiose, laminaribiose, melibiose, lactose, raffinose; salicin.
(*c*) Glycerol, DL-erythritol, D-arabitol, D-mannitol, D-sorbitol, *i*-inositol, DL-glyceraldehyde.
(*d*) 3-, 6-, 2 : 3-Di-, 2 : 3 : 6-tri- and 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose; 1 : 2-5 : 6-di-*O*-*iso*propylidene-D-glucose; D-glucose 6-phosphate; levoglucosan, 1 : 6-anhydro-α-D-glucofuranose.
(*e*) D-Fructose, D-galactose, D-arabinose, L-arabinose, D-rhamnose, L-fucose.
(*f*) D-Glucosamine hydrochloride, *N*-acetyl D-glucosamine.

The results are shown in Table 1, the relative efficiencies in causing a fall in iodine-staining power being computed on a molar basis. Such comparison assumes that only one hydroxyl group per acceptor molecule participates in the reaction. Having regard to the

* Part XXII, *J.*, 1956, 3025.

[1] Part XX, *J.*, 1956, 44.

structures of the substances showing positive response, this assumption is probably true for all with the possible exception of αα-trehalose. It is considered that any substance causing a fall in iodine-staining power greater than 5% (glucose, 100%) has significant acceptor activity. There were nine such substances, the most efficient being methyl α-D-glucoside. Although the evidence is insufficient to indicate the precise structural features required in an acceptor, attention may be drawn to certain points :

(1) The ideal acceptor appears to be α-D-glucopyranose and any departure from this structure is accompanied by a diminution, or by a complete loss, of acceptor activity. The most potent acceptor, after glucose, is methyl α-D-glucopyranoside (37%). It is suggested that the α-form of free glucose is more effective than the β-form because methyl α-glucoside is a better acceptor than is methyl β-glucoside (12%).

(2) Only a limited number of α-glucosides function as (weak) acceptors. These are maltose (11%), αα-trehalose (10%), and sucrose (6%). The α-glucosides, isomaltose, maltulose, melezitose, and glucose 1-phosphate, display no activity. Leucrose [*O*-α-D-glucopyranosyl-(1 ⟶ 5)-D-fructose] [2] appears to be a good acceptor (34% of the activity of glucose). Our specimen of leucrose was chromatographically pure and no explanation of its relatively high activity can be offered at present.

(3) Of those tested, the only β-glucoside which showed any acceptor activity was methyl β-D-glucoside (12%).

(4) The pyranose ring is an essential part of the acceptor structure. All the sugar alcohols tested, including D-sorbitol, were inactive, as was DL-glyceraldehyde.

(5) Substitution at any of the carbons atoms of glucose, apart from $C_{(1)}$, leads to complete loss of acceptor activity.

(6) Departure from the configuration of D-glucose also leads in most cases to complete loss of activity. The exceptions are D-mannose (13%), D-xylose (10%), and L-sorbose (10%), but even in these cases acceptor activity is seriously impaired. It may be significant to note that D-fructose, which might be considered closer in configuration to D-glucose than is L-sorbose, is devoid of acceptor activity.

There are four ways in which D-enzyme could transfer a portion of a maltodextrin chain to the acceptor. These are illustrated diagrammatically below. The donor substrate is N–R, N containing the non-reducing end and R the reducing end of the maltodextrin, and the acceptor substrate is A. If we consider the case in which A is glucose then there are two ways in which a compound of A and N could be formed. In the first (eqn. 1) the N–R bond is broken and N is joined through its liberated reducing group to the $C_{(4)}$-hydroxyl group of the glucose acceptor. Alternatively (eqn. 2), the glucose acceptor could be joined through its reducing group to $C_{(4)}$ of the non-reducing end glucose unit of the transferred fragment, N. The third and fourth reactions proceed in similar fashion except that the transferred portion of the donor is now the reducing fragment R.

$$N-R+A \rightleftharpoons N-A^{*}+R \quad \ldots\ldots\ldots\ldots \quad (1)$$

$$N-R+A \rightleftharpoons A-N^{*}+R \quad \ldots\ldots\ldots\ldots \quad (2)$$

$$N-R+A \rightleftharpoons R-A^{*}+N \quad \ldots\ldots\ldots\ldots \quad (3)$$

$$N-R+A \rightleftharpoons A-R^{*}+N \quad \ldots\ldots\ldots\ldots \quad (4)$$

(Reducing end of product marked with asterisk.)

In this type of transglycosylation it has been generally assumed that the reaction proceeds according to eqn. (1), and indeed equations (2) and (4) can be eliminated on the basis of our experiments on acceptor specificity which show that transfer to methyl α-glucoside occurs although $C_{(1)}$ is blocked by the methyl group. It seemed likely that the transfer occurred to the $C_{(4)}$-hydroxyl of the methyl glucoside, in which case incubation of a donor

[2] Stodola, Sharpe, and Koepsell, *J. Amer. Chem. Soc.*, 1956, **78**, 2514.

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substrate with D-enzyme and methyl α-glucoside should give methyl α-glucosidic derivatives of the maltodextrins. This experiment was carried out on a large scale with amylopectin as donor substrate. The products were fractionated by charcoal–Celite chromatography, and paper chromatography showed each fraction (di-, tri-saccharides, etc.) to consist of a reducing and a non-reducing substance. The reducing substances probably arose from the action of R-enzyme [3] and/or amylase on the linkages of the amylopectin. It is known that our D-enzyme preparations contained R-enzyme and a trace of amylase. Purification of the non-reducing di-, tri-, and tetra-saccharides was achieved by paper chromatography. The products (amorphous) were examined for specific optical rotation, methoxyl content, periodate uptake, and formic acid liberation, as well as for R_f value.

The methoxyl contents and periodate oxidation data (Table 2) agreed well with the values calculated on the assumption that the non-reducing di-, tri-, and tetra-

TABLE 2. *Properties of methyl α-maltoside, α-maltotrioside, and α-maltotetraoside.*

						IO_4^- oxidn.				
						Moles consumed		Moles $H{\cdot}CO_2H$ produced		
	R_f *		$[\alpha]_D^{18}$ in	MeO (%)						Priming
Glycoside	(*a*)	(*b*)	H_2O	Found	Calc.	Found	Calc.	Found	Calc.	activity †
α-Maltoside	0·37	0·19	+180°	8·68	8·75	3·06	3·0	1·02	1·0	0·1 (0)
α-Maltotrioside ...	0·28	0·09	+200	5·89	5·99	3·93	4·0	1·01	1·0	2·3 (2·1)
α-Maltotetraoside...	0·21	0·04	+213	4·58	4·56	5·02	5·0	1·01	1·0	9·0 (9·1)

* (*a*) R_f values in propan-1-ol–ethyl acetate–water (6 : 1 : 3); (*b*) R_f values in butan-1-ol–acetic acid–water (4 : 1 : 5).

† Towards phosphorylase–glucose 1-phosphate. Amounts of inorganic phosphate liberated, expressed in terms of colorimeter units (see Experimental section). Priming activities of equimolar amounts of the corresponding free sugars, measured at the same time, are given in parentheses.

saccharides were methyl α-maltoside, α-maltotrioside, and α-maltotetraoside. When plotted against degree of polymerisation both the molecular optical rotations and the $R_M\{= \log[(1/R_F) - 1]\}$ values showed a linear relation, indicative of uniformity of linkage.[4-7] The high optical rotations show that the polymeric linkages have the α-configuration. The periodate oxidation data eliminate the possibility of 1 : 3- or 1 : 6-linkages, leaving α-1 : 4- and α-1 : 2-linkages as the only possible types. Having regard to the mode of formation of these substances and the fact that they are degraded by starch-metabolising enzymes (see below) there is little doubt that the α-1 : 4-link is the only polymeric bond present. We are led to conclude therefore that these products are of the expected constitution and that D-enzyme action must proceed according to eqn. (1) or (3). Evidence will be presented later that eqn. (1) represents the course of the reaction.

It was of interest to compare the properties of the methyl maltodextrins with those of the free sugars in respect of the actions of various starch-metabolising enzymes. The priming activities towards the phosphorylase–glucose 1-phosphate system are closely similar to those of the corresponding free sugars.[8] That is, methyl α-maltoside had no priming activity, the trioside weak activity, and the tetraoside the same strong activity as maltotetraose (Table 2). β-Amylolysis of methyl α-maltotetraoside yielded maltose and methyl α-maltoside. Under the same conditions of low enzymic activity the methyl maltoside and maltotrioside were not attacked. The behaviour of the glycosides is therefore identical with that of the corresponding free maltodextrins.[4,9] Crystalline salivary

[3] Part XIV, *J.*, 1951, 1451; Part XIX, *J.*, 1954, 4440.
[4] Whelan, Bailey, and Roberts, *J.*, 1953, 1293.
[5] French, *Adv. Carbohydrate Chem.*, 1954, **9**, 149.
[6] Lindberg and McPherson, *Acta Chem. Scand.*, 1954, **8**, 985.
[7] Haq and Whelan, *J.*, 1956, 4543.
[8] Whelan and Bailey, *Biochem. J.*, 1954, **58**, 560.
[9] Whelan and Roberts, *ibid.*, 1954, **58**, 569.

α-amylase slowly attacked the methyl maltotrioside to give glucose and methyl maltoside, but maltose and methyl α-glucoside were not formed. This is in contrast to the action of α-amylase on maltotriose according to the experiments of Pazur and Budovich [10] which show that both linkages in maltotriose can be attacked by α-amylase, the more susceptible link being that which in the methyl maltotrioside is not readily attacked. α-Amylolysis of methyl α-maltotetraoside yielded large amounts of maltose and methyl maltoside together with small amounts of maltotriose and methyl glucoside. In agreement with Pazur [11] we found that maltotetraose yielded maltose as the major product, with small amounts of maltotriose and glucose. Whelan and Roberts in a similar experiment [12] failed to detect the formation of glucose and maltotriose.

Experimental

Measurement of Activity of D-Enzyme.—The measurement made was that of glucose liberated during the action of D-enzyme in maltotriose. The digest contained maltotriose (60 mg.), 0·2M-citrate buffer (pH 7·0; 0·3 ml.), and enzyme in a total of 3 ml. After incubation for 30 min. at 35° the enzyme was inactivated by heat, and the digest transferred to a charcoal–Celite column (1 : 1, w/w; 6·0 × 1·5 cm.) and eluted with water. The first 5 ml. of eluate were discarded. The next 25 ml. were collected, passed through a Seitz filter, and the optical rotation of the eluted glucose measured in a 4-dm. tube. A linear relation was observed between glucose liberated and concentration of enzyme in the range 0—9 mg. of glucose. One unit of enzyme was defined as the amount required to liberate 1 mg. of glucose under these conditions.

Preparation of D-Enzyme.—The method used is based on observations made by the late Mr. G. W. F. Kroll. These are (i) that the addition of a small amount of copper sulphate to the ammonium sulphate used in precipitating D-enzyme from potato juice effectively eliminates phosphorylase activity, and (ii) that repeated precipitation of the D-enzyme fraction with ammonium sulphate largely destroys its Q-enzyme activity.

To charcoal-clarified potato juice [1] (540 ml.) was added copper sulphate (1 g.) and 50% (w/w) ammonium sulphate solution (pH 7·0; 460 ml.) giving a final ammonium salt concentration of 23% (w/v). After the solution had been kept for 24 hr. at 2° the precipitate was removed on the centrifuge, dissolved in 0·01M-citrate buffer (pH 7·0, 250 ml.), and precipitated by the addition of ammonium sulphate to 20% (w/v) concentration. After 24 hr. at 2° the precipitate was removed, redissolved, and re-precipitated twice, as before except that it was kept for only 2 hr. before centrifugation. The final product was taken up in 0·2M-citrate buffer (pH 7·0; 50 ml.) and freeze-dried. The amounts of enzyme obtained after the second, third, and fourth precipitations were 1720, 1370, and 1036 units, respectively, while the specific activities, expressed as units of enzyme/mg. of protein nitrogen were 1·05, 1·78, and 2·33, respectively.

Acceptor Specificity of D-Enzyme.—The donor substrate, a mixture of maltodextrins ranging in degree of polymerisation from about 5 to 10, was prepared as follows. Potato amylose [13] (5·6 g.) was dissolved in warm 0·7N-sodium hydroxide (170 ml.), the solution neutralised to phenolphthalein with 3N-sulphuric acid, and a further 30 ml. of acid added. The solution was heated on a boiling-water bath until a small portion gave no colour with iodine. Then the solution was cooled quickly, neutralised (NaOH), and transferred to a charcoal–Celite column (1 : 1, w/w; 43 × 7·5 cm.), which was irrigated with water (2 l.) and then 20% aqueous ethanol until optically active material was no longer desorbed. Thereafter 50% ethanol was used as the eluant and the optically active eluate so obtained was evaporated to dryness, and inorganic matter largely removed by dissolving the dextrins in 80% aqueous methanol, and filtering and again evaporating the solution, to yield about 1 g. of product.

D-Enzyme (1036 units, see above) was dissolved in 0·2M-citrate buffer (pH 7·0; 50 ml.) and a portion (5 ml.) was incubated at room temperature with the mixed maltodextrins (300 mg.; 10 ml.). Portions (0·2 ml.) of the digest were added to iodine solution (0·005% in 0·05% of potassium iodide solution; 6 ml.) and the absorption value recorded in an E.E.L. colorimeter having 1·3 cm. diameter cells and a no. 404 filter (wavelength of peak transmission, 510 mμ).

[10] Pazur and Budovich, *Science*, 1955, **121**, 702.
[11] Pazur, *J. Biol. Chem.*, 1953, **205**, 75.
[12] Whelan and Roberts, *J.*, 1953, 1298.
[13] Part XIII, *J.*, 1951, 801.

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After digestion for 5 hr. the solution had constant absorption value, and portions (0·2 ml.) were added to weighed amounts (approx. 10 mg.) of the acceptor substance in colorimeter tubes, which were kept for 13 hr. at constant temperature before being treated with iodine solution (6 ml.), and the light absorption measured. The values so obtained were compared with that of a digest portion to which no acceptor had been added and the fall in iodine stain, if any, was compared on a molar basis with that induced by glucose, reckoned as 100% (see Table 1). It had been shown that a direct proportionality existed between weight of glucose added and fall in iodine-staining power, within the weight range of sugar concentration employed.

Action of D-Enzyme on Amylopectin and Methyl α-Glucoside.—A solution of potato amylopectin [13] (24 g.) in warm 0·1N-sodium hydroxide (750 ml.) was cooled, neutralised (phenolphthalein) with N-sulphuric acid, and diluted to 1950 ml. Methyl α-glucoside (20 g.) was then added, followed by D-enzyme (prepared as above from 5 kg. of " Majestic " potatoes) in 50 ml. of 0·2M-citrate buffer (pH 7·0). The digest was incubated at 20° with one of similar composition (10 ml.) except for the omission of methyl α-glucoside. Absorption values of iodine-stained portions (0·2 ml.) were measured as before, by use of an E.E.L. colorimeter with an Ilford filter no. 608 (peak transmission, 680 mμ). Expressed as a percentage of the original absorption the values after incubation for 6, 17½, 39, 66, and 90 hr. were, respectively (glucoside digest given first), 84·5, 93; 74·5, 89·5; 64·5, 85·5; 57·5, 82·5; 52·5, 81%. At 90 hr. ethanol (8 l.) was added to the main digest and 1 hr. later the precipitate was removed on the centrifuge and washed with 80% ethanol (2 l.), and the combined supernatant liquid filtered and evaporated to dryness at 40°. The residue was dissolved in water (250 ml.) and a portion examined by paper chromatography in propan-1-ol–ethyl acetate–water (6 : 1 : 3, by vol.). When sprayed with silver nitrate–sodium hydroxide solution [14] there were revealed a series of reducing and a series of non-reducing sugars. The reducing sugars correspond to glucose and the maltodextrins. The reducing power of the solution was equivalent to 416 mg. of glucose (from 24 g. of amylopectin). At this stage we attempted to oxidise the reducing sugars with alkaline iodine by Kline and Acree's method,[15] barium hydroxide being used in place of sodium hydroxide, in the hope that the methanol-insoluble barium salts of the sugar acids could be removed. However, only half the expected amount of iodine was consumed. The pH was then adjusted to 6·0 (N-sulphuric acid) and the solution taken to dryness and extracted with hot methanol (2·5 l.). The evaporated extract was dissolved in water (150 ml.); chromatographic examination showed that reducing sugars were still present. Consequently the solution was adsorbed on charcoal–Celite (1 : 1, w/w; 165 × 6 cm.) and eluted by the gradient method,[16] a reservoir of water (20 l.) above the column being kept at constant level by the addition of 40% ethanol. Fractions (250 ml. each) were collected and their optical rotation measured in a 4-dm. tube. The optical rotation returned to zero after each of the first three peak values was attained. Thereafter the resolution became increasingly less complete. The eluate fractions were combined in 9 batches which displayed the following properties (for the purposes of easier description the substances revealed by paper chromatography are named in terms of their subsequently identified structure): (*a*) 4·2—6·4 l. of eluate in order of collection, 12·1 g. of methyl α-glucoside; (*b*) 9·0—10·0 l., 0·80 g. of methyl α-maltoside + maltose; (*c*) 10·0—12·2 l., 1·81 g. of methyl α-maltoside and a trace of maltose; (*d*) 13·9—17·8 l., 2·10 g. of methyl α-maltotrioside + maltotriose; (*e*) 18·5—20·6 l., 1·10 g. of methyl α-maltotetraoside + maltotetraose; (*f*) 20·9—22·3 l., 0·75 g. of methyl α-maltotetraoside, α-maltopentaoside, and a trace of maltopentaose; (*g*), (*h*), and (*i*), 22·3—28·2 l., total wt. 1·52 g. of methyl α-maltopentaoside, maltopentaose, and higher reducing and non-reducing oligosaccharides. Separation of the non-reducing from reducing sugars was achieved by chromatography of portions of batches (*b*)—(*e*) on Whatman no. 3 paper in butan-1-ol–acetic acid–water (4 : 1 : 5, by vol.). In this way chromatographically pure specimens of methyl glycosides of the di-, tri-, and tetrasaccharides were obtained. Solutions in hot 80% methanol were filtered and taken to dryness, the residues dissolved in water (50 ml.), such solutions treated with Somogyi's deproteinising reagents [17] and freeze-dried, and the products finally dissolved in 50 ml. of water. All measurements of properties of the sugars were made on portions taken from these solutions.

Properties of the Methyl Maltodextrins.—The amounts of dextrin present were estimated by

[14] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[15] Kline and Acree, *Ind. Eng. Chem. Anal. Edn.*, 1930, **2**, 413.
[16] Alm, *Acta Chem. Scand.*, 1952, **6**, 1186.
[17] Somogyi, *J. Biol. Chem.*, 1945, **160**, 69.

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acid hydrolysis [18] to glucose. The molecular weights of the dextrins being assumed, the final weights of purified materials were: methyl α-maltoside, 47·5 mg.; methyl α-maltotrioside, 132 mg.; and methyl α-maltotetraoside, 254 mg.

(a) *Reducing power.* When heated with Somogyi reagent [19] for 45 min., portions (5 mg.) of the malto-trioside and -tetraoside developed no detectable reducing power while the methyl maltoside had reducing power equivalent to 1% of that of an equal weight of maltose.

(b) *Methoxyl content.* Volumes of solution containing from 9 to 25 mg. of glycoside were taken to dryness in the reaction vessel of the apparatus described by Milton and Waters.[20] Methoxyl content was then determined as described by Belcher, Fildes, and Nutten [21] (see Table 2).

(c) *Periodate oxidation.* The glycosides were oxidised in 12·5mM-sodium metaperiodate, in the dark at room temperature. Consumption of periodate was measured after 24 hr. and 48 hr. by adding portions of digest to acidified potassium iodide and titrating with 0·05N-thiosulphate. Formation of formic acid was measured at the same times by addition of neutral potassium iodide to portions of digest after removal of periodate with ethylene glycol. 5mN-Thiosulphate was used to titrate the iodine liberated. Oxidation was complete after 24 hr. (Results are given in Table 2.)

(d) *Action of enzymes.* In the test for phosphorylase priming activity the digests contained glucose 1-phosphate (2 ml.; 0·1M; pH 7·07), citrate buffer (1 ml.; pH 7·0), ammonium molybdate (0·1 ml., 8·3%), mercuric chloride [22] (0·1 ml., 0·004%), methyl glycoside (1 μmole), freeze-dried potato phosphorylase [8] (1 ml., 50 mg.), and water to 6 ml. The enzyme solution (at 35°) was added last to the mixture of components maintained at 35°. A primer-free digest was also included. After 30 min., a portion (0·2 ml.) was removed from each digest for measurement of inorganic phosphate by Whelan and Bailey's method.[8] The results given in Table 2 are corrected for the phosphate content of the primer-free digest.

For α-amylolysis portions (20 mg.) each of the trioside, tetraoside, maltotriose, and maltotetraose were incubated separately for 30 min. at 30° in 2 ml. of 0·05M-acetate buffer (pH 7·0) containing 1 drop of a suspension of crystalline human salivary α-amylase,[23] kindly provided by Professor Jytte Muus. The enzyme was inactivated by heat and paper chromatographic examination was carried out in propan-1-ol–ethyl acetate–water as described above.

β-Amylolysis was carried out as for α-amylolysis except that the pH was 4·8. The enzyme was purified soya-bean β-amylase,[24] in amount insufficient to hydrolyse the maltotriose during 30 minutes' incubation (cf. Whelan, Bailey, and Roberts [4]).

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University College of North Wales, Bangor.
The Lister Institute, London, S.W.1.

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[18] Pirt and Whelan, *J. Sci. Food Agric.*, 1951, **2**, 224.
[19] Somogyi, *J. Biol. Chem.*, 1945, **160**, 61.
[20] Milton and Waters, "Methods of Quantitative Micro-Analysis," Edward Arnold, London, 1949, p. 113.
[21] Belcher, Fildes, and Nutten, *Analyt. Chim. Acta*, 1955, **13**, 16.
[22] Bailey, Thomas, and Whelan, *Biochem. J.*, 1951, **49**, lvi.
[23] Muus, *Compt. rend. Trav. Lab. Carlsberg*, 1953, **28**, 317.
[24] Part XVI, *J.*, 1952, 714.

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486. *Olefin Co-ordination Compounds. Part IV.* Diene Complexes of Platinum*(II). *The Structure of Hofmann and von Narbutt's* [*Dicyclopentadiene*(RO)PtCl].

By J. Chatt, (Miss) L. M. Vallarino, and L. M. Venanzi.

A number of chelate complexes of the type [dienePtX_2] (X = halogen) (V) have been prepared. Of the dienes used, the stabilities of the complexes are in the order, *cyclo*octa-1 : 5-diene $\simeq$ di*cyclo*pentadiene > dipentene > hexa-1 : 5-diene. The stabilities of the dihalides decrease in the order Cl > Br > I. The dithiocyanate is not of the same type, and perhaps it should be formulated as [dienePt$(SCN)_2$Ptdiene]$(SCN)_2$.

With anhydrous sodium carbonate in alcohol the dihalides give crystalline, stable alkoxy-halides (dieneOR)$_2$Pt$_2$X$_2$ (Table 1) of structure (X) in which one double bond has been opened by Pt(OR)X and the other is co-ordinated to the metal. The di*cyclo*pentadiene methoxy-chloride [$(C_{10}H_{12}OMe)_2Pt_2Cl_2$] is especially easy to prepare; its chlorine atoms are readily replaced by I^-, SCN^-, and SEt^-, but the methoxy-group is very firmly bound. *p*-Toluidine splits the halogen bridge to give monomeric [$C_{10}H_{12}OMe,C_7H_9NPtCl$]. The corresponding iodide does not react with *p*-toluidine. The methoxy-group can be replaced by boiling concentrated hydrochloric acid to reform [$C_{10}H_{12}PtCl_2$]. The compounds are thus analogous to the alkoxymercuric compounds formed from olefins and mercuric salts, but are much more stable to hydrochloric acid.

A few peculiar *cyclo*octa-1 : 5-diene derivatives approximating to [$C_8H_{12}Pt(OR)_2]_n$ (R = Me and H) were discovered but not investigated.

When dienes (diolefins) react with platinous salts, *e.g.*, K_2PtCl_4, in water or aqueous alcohol, three types of reaction may occur. (*a*) Platinum or some other decomposition products may be produced as with hexa-2 : 4-diene.[1] (*b*) The double bonds may react independently with different platinum atoms to give complex salts, as does butadiene :[2]

$$C_4H_6 + 2K_2PtCl_4 \longrightarrow K_2[C_4H_6(PtCl_3)_2] + 2KCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

(*c*) The olefin may chelate to one platinum atom, as does dipentene [3] [reaction (2)] and *cyclo*-octatetraene.[4] Only two double bonds of the tetraene are attached to the platinum atom. The three types of reaction are not mutually exclusive and indeed hexa-1 : 5-diene reacts according to either (*b*) or (*c*) depending on the conditions of the reaction.[1, 5]

$$C_{10}H_{16} + K_2PtCl_4 \longrightarrow [C_{10}H_{16}PtCl_2] + 2KCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Apart from the above dienes, *cyclo*octa-1 : 5-diene (I) and di*cyclo*pentadiene (II) are of special interest at the present time: the former because it forms the most stable olefin complexes yet discovered, and the latter because it is known to yield what are apparently alkoxy-chlorides with potassium chloroplatinite in aqueous methanol or ethanol.[6, 7]

Alkoxy-complexes are otherwise unknown in the complex chemistry of platinum, and attempts to prepare them usually cause decomposition. We have therefore examined the non-ionic platinous halide complexes of *cyclo*octa-1 : 5-diene (I), di*cyclo*pentadiene (II), and dipentene (III). In general formulæ, the dienes are being represented by the symbol (IV). We found that under very mild conditions the complexes can be converted into

* Part III, *J.*, 1953, 2939.

[1] Jensen, *Acta Chem. Scand.*, 1953, **7**, 866.
[2] Hel'man, *Compt. rend. Acad. Sci., U.R.S.S.*, 1939, **23**, 532.
[3] Chatt and Wilkins, *J.*, 1952, 2622.
[4] Jensen, *Acta Chem. Scand.*, 1953, **7**, 868.
[5] Hel'man, *Compt. rend. Acad. Sci., U.R.S.S.*, 1941, **32**, 347.
[6] Hofmann and von Narbutt, *Ber.*, 1908, **41**, 1625.
[7] Doyle and Jonassen, *J. Amer. Chem. Soc.*, 1956, **78**, 3965.

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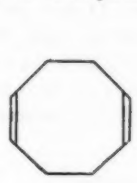
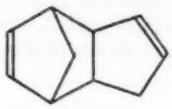
alkoxy-halides, with an ease varying from case to case. The di*cyclo*pentadiene complexes yield the alkoxy-compounds most readily.

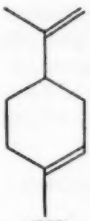
Diene Complexes of Platinous Halides.—Diene complexes [dienePtCl$_2$] were prepared by previous workers by treating aqueous-alcoholic solutions of chloroplatinites with the diene. We find that they are more conveniently prepared in organic solvents such as the lower alcohols, particularly propan-1-ol. The chelate complex crystallises from the mixture in 2—3 days at room temperature.



(I)



(II)

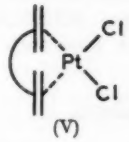


(III)

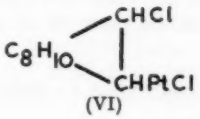
(IV)

The dibromo- and di-iodo-complexes are readily obtained by treating the dichloro-complexes with lithium bromide and lithium iodide respectively in hot acetone. The bromides may also be obtained directly by adding lithium bromide to the reaction mixture used to prepare the chlorides, but the iodides are less stable and better prepared from the chlorides. Two dipentene complexes [dipentenePtCl$_2$] are known,[3, 8] and the one obtained by the above method is identical with Chatt and Wilkins's β-isomer. The di*cyclo*pentadiene complex $C_{10}H_{12}PtCl_2$ obtained as above is identical with the compound $C_{10}H_{12}PtCl_2$ to which Hofmann and von Narbutt [6] ascribed structure (VI).

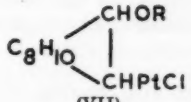
The diene complexes [dienePtX$_2$] (X = halogen), are monomeric, and non-electrolytes in nitrobenzene; they are best formulated as chelate complexes of type (V).[1, 3, 4, 7] They are very much more stable than the platinous complexes of mono-olefins, and their stabilities decrease in the order Cl > Br > I, in accordance with the increasing *trans*-effect of the halogens Cl < Br < I. In contrast with the complexes of mono-olefins the diene complexes do not darken immediately on contact with slightly alkaline water, and give colourless solutions in dilute aqueous sodium hydroxide; these darken and deposit black decomposition products.[9] *cyclo*Octadiene (I) and di*cyclo*pentadiene (II) in which the double bonds are suitably placed for chelation form exceptionally stable complexes. Dipentene (III), where various conformations of the diene are possible, gives rather less stable complexes. Hexa-1 : 5-diene, where the double bonds can be arranged relatively as in *cyclo*octadiene but are not fixed rigidly, gives still less stable complexes.



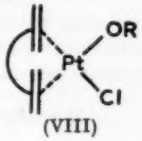
(V)



(VI)



(VII)



(VIII)

The *cyclo*octadiene complex [$C_8H_{12}PtCl_2$] can also be prepared, but more slowly, by using sodium chloroplatinate instead of the platinite in the above preparation.

A dithiocyanate [$C_{10}H_{12}Pt(SCN_2)]_x$, very sparingly soluble in all the solvents tried, has been examined in a preliminary way and has a structure different from that of the dihalides. Its infrared spectrum, kindly measured by Dr. L. A. Duncanson, has very strong absorption bands at 2159 and 2055 cm.$^{-1}$; these can be due only to the thiocyanate groups and indicate that there are two types of such groups in the structure. The SCN$^-$ ion in

[8] Kharasch and Ashford, *J. Amer. Chem. Soc.*, 1936, **58**, 1733.

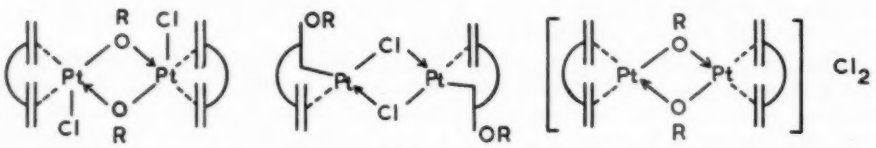
[9] K. A. Jensen, Conference on Co-ordination Chemistry, Copenhagen, 1953; his diolefin compounds dissolved in alkali.

potassium thiocyanate absorbs at 2063 cm.$^{-1}$, terminal thiocyanate groups in platinous complexes in the range 2100—2120 cm.$^{-1}$, and bridging thiocyanate groups in platinous complexes in the range 2150—2182 cm.$^{-1}$.[10] It appears therefore that the dithiocyanate contains bridging and ionic thiocyanate groups. This suggests a formula such as $[C_{10}H_{12}Pt(SCN)_2PtC_{10}H_{12}](SCN)_2$.

Alkoxy-derivatives of the Diene Complexes.—In 1908 Hofmann and von Narbutt [6] described three compounds obtained by the reaction of di*cyclo*pentadiene with potassium chloroplatinite in aqueous alcohol at 35°. The reaction required 10—14 days and yielded, from aqueous methanol and ethanol, compounds of the composition $C_{10}H_{12}Pt(OMe)Cl$ and $C_{10}H_{12}Pt(OEt)Cl$ respectively, but from aqueous propanol they isolated the dichloride. These they formulated as addition products (VII) and (VI) respectively, from analogy with the compounds formed by mercuric salts and olefins in alcoholic solution, where reaction occurs as follows : [11]

$$C_2H_4 + Hg(OAc)_2 + EtOH \longrightarrow EtO{\cdot}CH_2{\cdot}CH_2{\cdot}Hg{\cdot}OAc + AcOH$$

These structures do not accord with our present knowledge of platinous chemistry, for platinum(II) never has a co-ordination number of less than four. The dihalides definitely have the structure (V), but the analogous structure (VIII) for the alkoxy-halides can be ruled out because they are dimeric. There appear to be three other possible types of structure (IX), (X), and (XI). In (IX), the alkoxy-groups are bridging groups and the chlorine atoms occupy fifth, or if they are also bridging groups, fifth and sixth positions on the platinum atoms. Such structures are theoretically possible. In (X), one double bond has been



(IX) (X) (XI)

saturated so that effectively Pt(OR)Cl has been added across the double bond. In (XI), the methoxyl groups are bridging groups and the chlorine is ionic. Our experiments lead us to structure (X), and so we have formulated them as, for example, $(C_{10}H_{12}OR)_2Pt_2Cl_2$ rather than $(C_{10}H_{12})_2Pt_2(OR)_2Cl_2$ in the following description of their reactions and properties.

Preparation of the Alkoxy-derivatives, $[(dieneOR)_2Pt_2X_2]$.—Hofmann and von Narbutt's method is slow and of limited applicability. We find, however, that the alkoxy-derivatives can be most readily prepared by the reaction of the dihalogen complexes, $[dienePtX_2]$, with the appropriate alcohol used as solvent, in the presence of a weak base such as anhydrous sodium carbonate or acetate :

$$2[dienePtX_2] + 2ROH + 2Na_2CO_3 \longrightarrow [(dieneOR)_2Pt_2X_2] + 2NaX + 2NaHCO_3$$

Stronger bases such as sodium alkoxide react similarly, but they cause some decomposition if used in excess of the equivalent proportions.

Di*cyclo*pentadiene–alkoxy-complexes are very readily obtained (doubtless because saturation of a double bond releases some strain in the *cyclo*pentene ring system), but those of the other dienes more difficultly, and the conditions are more critical. Methoxy-chloro-complexes, $[(dieneOMe)_2Pt_2Cl_2]$ of all the cyclic dienes were prepared, and various alkoxychloro-complexes of di*cyclo*pentadiene (see Table).

Properties of the Alkoxy-derivatives.—In spite of containing carbon and platinum(II)

[10] Chatt and Duncanson, *Nature*, 1956, **178**, 997.
[11] See Chatt, *Chem. Rev.*, 1951, **48**, 7.

in direct combination, the alkoxy-chlorides are remarkably stable. They are insoluble in water, but are soluble to varying degress in organic solvents, notably chloroform. They are dimeric and non-electrolytes in nitrobenzene solution, so ruling out structure (XI). The reactions of the compound $[(C_{10}H_{12}OMe)_2Pt_2Cl_2]$ were studied as a representative member of the series.

Alkoxy-derivatives of the diene complexes of platinum(II).

Compound	Decomp. pt.	
$(C_{10}H_{12}OMe)_2Pt_2Cl_2$	205—220°	White plates
$(C_{10}H_{12}OMe)_2Pt_2I_2$	190—220	Pale yellow plates
$(C_{10}H_{12}OMe)_2Pt_2(SCN)_2$	260—270	White plates
$(C_{10}H_{12}OMe)_2Pt_2(SEt)_2$	145—146 *	Pale yellow needles
$(C_{10}H_{12}OMe)$, *p*-toluidinePtCl	160—170 *	White needles
$(C_{10}H_{12}OEt)_2Pt_2Cl_2$	200—220	White plates
$(C_{10}H_{12}OPr^n)_2Pt_2Cl_2$	205—215	White plates
$(C_9H_{12}OMe)_2Pt_2Cl_2$	150—170	White powder
$(C_9H_{12}OMe)_2Pt_2I_2$	150—160	Cream needles
$(C_9H_{12}OMe)$, *p*-toluidinePtCl	140—142 *	White needles
$(C_{10}H_{14}OMe)_2Pt_2Cl_2$	135—145	Cream needles

* Melts to an oil which does not solidify again.

The chlorine atoms are very readily replaced by anions such as iodide, thiocyanate, and EtS^- by treating methanolic or acetone solutions of the alkoxy-chloride with lithium iodide, sodium thiocyanate, or sodium ethyl sulphide respectively, *e.g.*, :

$$[(C_{10}H_{12}OMe)_2Pt_2Cl_2] + 2LiI \longrightarrow [(C_{10}H_{12}OMe)_2Pt_2I_2] + 2LiCl$$

In these reactions the chlorine atom is readily replaced by the anions I^- and SCN^- whose affinity for platinum exceeds that of Cl^-.[12] On the other hand, the methoxyl group which normally has a very poor affinity for platinum(II) remains in the molecule. This suggests that the halogen may be attached to the platinum atom and that the methoxyl group is not. Even the SEt^- ion, which is the strongest bridging group known in platinous chemistry,[13] failed to displace the methoxyl group, which suggests that it is not a bridging group, as required by structures (IX) and (XI).

The methoxyl group is very firmly bound in the complex, but Hofmann and von Narbutt showed that it is removed, to yield the dichloride $[C_{10}H_{12}PtCl_2]$, by boiling concentrated hydrochloric acid in 3—4 hours. We confirm this. The resistance to hydrochloric acid is also evidence that the methoxyl group is not attached to the platinum atom. The methoxyplatinous compounds have evidently much greater resistance to hydrochloric acid than the methoxymercurials, which immediately evolve the olefin in cold dilute hydrochloric acid, but the mechanism of the elimination of the methoxyl group is probably similar,[14, 15] except that the resulting olefin complex, $[C_{10}H_{12}PtCl_2]$, is a stable product in hydrochloric acid, whereas the mercuric complexes, $[olefinHgCl]^+$ or such, decompose immediately in dilute hydrochloric acid.

It is well established that chloro-bridged platinous complexes are readily " split " by *p*-toluidine to monomeric complexes according to the following scheme (L = an uncharged ligand) :

$$[L_2Pt_2Cl_4] + 2p\text{-Toluidine} \rightleftharpoons 2[L,p\text{-toluidinePtCl}_2]$$

and that the equilibrium lies well to the right-hand side. In the case of iodo-bridged complexes, however, the equilibrium lies so far to the left-hand side that the mixed product cannot always be isolated.[16]

[12] Leden and Chatt, *J.*, 1955, 2936.
[13] Chatt and Hart, *J.*, 1953, 2363.
[14] See Chatt, *Chem. Rev.*, 1951, **48**, 39.
[15] Brandt and Plum, *Acta Chem. Scand.*, 1953, **7**, 97.
[16] Chatt and Venanzi, *J.*, 1955, 3858.

XUM

We found similar behaviour with the di*cyclo*pentadiene complexes $[(C_{10}H_{12}OMe)_2Pt_2X_2]$. The methoxy-chloride reacted readily with *p*-toluidine to give a monomeric product :

$$[(C_{10}H_{12}OMe)_2Pt_2Cl_2] + 2C_7H_9N \longrightarrow 2[C_{10}H_{12}OMe,C_7H_9NPtCl]$$

but the methoxy-iodide was recovered unchanged on attempted reaction with *p*-toluidine. Further, on attempting to replace the chlorine (or methoxyl) in the monomeric $[C_{10}H_{12}OMe,C_7H_9NPtCl]$ by reaction with lithium iodide, both the chlorine and *p*-toluidine were eliminated, indicating that the compound $[C_{10}H_{12}OMe,C_7H_9NPtI]$ is unstable and readily reverts to the bridged iodo-complex :

$$2[C_{10}H_{12}OMe,C_7H_9NPtCl] + 2KI \longrightarrow 2[C_{10}H_{12}OMe,C_7H_9NPtI] \longrightarrow [(C_{10}H_{12}OMe)_2Pt_2I_2] + 2C_7H_9N$$

This behaviour accords with our knowledge of the reaction of amines with halogen-bridged platinous (and palladous) complexes. There can be no doubt, therefore, that the dimerisation of the alkoxy-halide takes place through halogen bridges only.

The most probable structure according with these facts is (X). The *trans*-arrangement of co-ordinated double bonds about the $PtCl_2Pt$ ring was confirmed in the case of $[(C_{10}H_{12}OPr^n)_2Pt_2Cl_2]$ and $[(C_{10}H_{16}OMe)_2Pt_2Cl_2]$ by determining $\Delta\varepsilon/f$ in benzene solution, ($\Delta\varepsilon$ = the increment in dielectric constant caused by the solute and f the mole fraction of solute).[17] The low values of 9·1 and 12·3 respectively leave no doubt about the *trans*-arrangement as shown in (X).

This conclusion is supported by the infrared spectra of the methoxy-thiocyanate and of the dipentene complexes, and we are indebted to Dr. L. A. Duncanson for his examination and interpretation. The methoxy-thiocyanate $[(C_{10}H_{12}OMe)_2Pt_2(SCN)_2]$ has a strong absorption band at 2158 cm.$^{-1}$, but none in the region 2100—2120 cm.$^{-1}$, indicating that the thiocyanate groups are bridging (see p. 2498).

Dipentene, $C_{10}H_{16}$, itself has a single strong band at 1674 cm.$^{-1}$ due to the C=C stretching modes. The complex $[C_{10}H_{16}PtCl_2]$ has a strong absorption band at 1512 cm.$^{-1}$ which can be assigned to these modes modified by co-ordination to the platinum atom : the lowering of 135 cm.$^{-1}$ caused by co-ordination is of the same order as the 143 cm.$^{-1}$ difference between the C=C frequency of gaseous propene and its platinous chloride complexes.[18] The only absorption band in the 1500—2000 cm.$^{-1}$ region of the spectrum of $[(C_{10}H_{16}OMe)_2Pt_2Cl_2]$ is a comparatively weak one at 1505 cm.$^{-1}$, and the remainder of the spectrum is altered considerably from that of the dichloride, $[C_{10}H_{16}PtCl_2]$.

It is evident that in dipentene and in $[C_{10}H_{16}PtCl_2]$ the two double bonds give absorption bands which are not resolved. The absorption due to the terminal $C{=}CH_2$ bond will be much more intense than that due to the more symmetrical double bond in the ring, and together they give the strong bands observed at 1647 and 1512 cm.$^{-1}$ in the spectra of dipentene and of its platinous chloride complex respectively. In the methoxy-complex the strongly absorbing $C{=}CH_2$ is destroyed by the addition of MeO and PtCl across the double bond, leaving the weakly absorbing endocyclic double bond; and since the latter absorbs at 1505 cm.$^{-1}$ it must be co-ordinated to the metal.

If in analogy with the methoxymercurials, we can assume that the platinum atom has attached itself to the CH_2 group of the double bond, the dipentene complex $[(C_{10}H_{16}OMe)_2Pt_2Cl_2]$ must have the structure (XII).

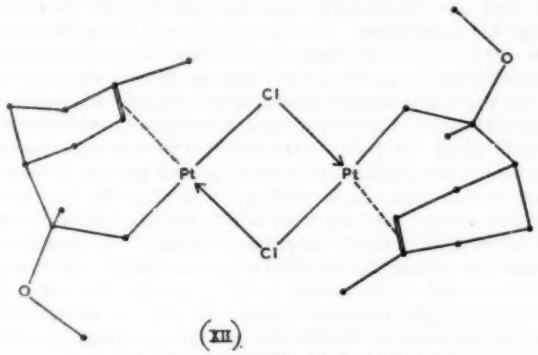
There can be little doubt that the alkoxy-derivatives of the $[dienePtCl_2]$ complexes are truly organometallic platinum compounds in which the metal has a valency of two and its normal co-ordination number of four. It might be argued against this that platinous alkyls are unknown and therefore very probably unstable. However, when the platinum(II) atom is co-ordinatively saturated, the alkyls may be stable. *E.g.*, Chatt and Foss [19] have prepared a platinous methyl, $(PPr^n_3)_2PtMeI$, which melts without decomposition at 48°, and is stable in air and to hydrolysis by dilute acids. During three years

[17] Chatt and Wilkins, *J.*, 1953, 70.
[18] Chatt and Duncanson, *J.*, 1953, 2939.
[19] Chatt and Foss, unpublished work.

XUM

in store, it has not decomposed. It seems possible that platinum(II), when it is so co-ordinatively saturated, might have an organic chemistry somewhat similar to that of mercury(II).

Dimethoxy- and Dihydroxy-derivatives of [dienePtCl$_2$].—Attempts to replace both halogen atoms in [$(C_{10}H_{12}OR)_2Pt_2Cl_2$] by reaction with sodium methoxide lead to the formation of black decomposition products. This is the usual result when one attempts



(XII)

Proposed structure of [$(C_{10}H_{14}OMe)_2Pt_2Cl_2$].
(The configurations about asymmetric centres are arbitrarily chosen.)

to attach a methoxyl group to platinum(II). However, a number of compounds which do not contain halogen, and appear to bear some relation to dimethoxy- and dihydroxy-derivatives were obtained in the above research. They were only cursorily investigated but are recorded.

A substance of composition approximating closely to [$C_8H_{12}Pt(OMe)_2]_n$ ($n > 2$, perhaps 3 or 4) separates when [$C_8H_{12}PtCl_2$] in methanol is treated with anhydrous sodium carbonate. This " α-dimethoxide " is soluble in hot methanol and crystallises in needles. If it is left in the reaction mixture at −70° for 24—48 hours, the dimethoxide is converted into [$(C_8H_{12}OMe)_2Pt_2Cl_2$]. The iodide [$C_8H_{12}PtI_2$] by a similar reaction does not give a dimethoxide but gives [$(C_8H_{12}OMe)_2Pt_2I_2$] directly.

A substance giving analyses as for [$C_8H_{12}Pt(OH)_2]_x$ was obtained by direct reaction of the *cyclo*octadiene with sodium chloroplatinite in methanol in the presence of anhydrous sodium carbonate. Its infrared spectrum showed no absorption bands in the OH stretching region, and the substance should perhaps be formulated in some way with oxide or ether bridges. In dilute aqueous sodium hydroxide it gives a clear solution which is much more stable than that given by the dichloride. On treatment with sodium carbonate in boiling methanol the " dihydroxide " is converted into a substance of composition approximating to [$C_8H_{12}Pt(OMe)_2]_x$, " β-dimethoxide," and different from the " α-dimethoxide." This substance is almost insoluble in hot methanol and crystallises in plates. The above three substances are crystalline, but the " dimethoxides " darken on storage for some weeks. They are soluble in chloroform, benzene and such organic solvents, but the " dihydroxide " is less soluble and was recrystallised from glacial acetic acid.

In all these substances it seems improbable that the oxygen is attached to the platinum atom. It is more likely to be bound to carbon only.

Experimental

Microanalyses are by Messrs. W. Brown and A. G. Olney of these laboratories.

Dicyclopentadienedichloroplatinum, [$C_{10}H_{12}PtCl_2$].—*Dicyclo*pentadiene (4 c.c.) was added to a solution of sodium chloroplatinite tetrahydrate (4 g.) in propan-1-ol (80—100 c.c.) and kept at room temperature for 2 days. The crystals which separated were filtered off, washed with

ether and then water, and dried. The compound was purified by dissolving it in hot chloroform, treating the solution with a small amount of charcoal, filtering it, and diluting the filtrate with ether. It was obtained in white needles (3·2 g.), decomp. 200—220° (Found: C, 30·0; H, 3·1. Calc. for $C_{10}H_{12}Cl_2Pt$: C, 30·2; H, 3·0%).

This reaction also occurs in methanol or ethanol but gives rather poorer yields, and in methanol the reaction is appreciably slower.

*Di*cyclo*pentadienedibromoplatinum*, $[C_{10}H_{12}PtBr_2]$, was prepared and purified analogously to the chloride, but with the addition of lithium bromide (2 g.) to the reaction mixture. The reaction takes 5 days for completion. The product (0·98 g.) was obtained in canary-yellow prisms, decomp. 200—225°. It is also obtained as follows: Di*cyclo*pentadienedichloroplatinum (0·45 g.) and lithium bromide (0·5 g.) in acetone (approx. 20 c.c.) were boiled for a few minutes. The complex dissolved and the dibromide separated on cooling. The yield of pure product was 0·41 g. and it was identical (infrared spectrum) with that obtained above (Found: C, 24·7; H, 2·65. $C_{10}H_{12}Br_2Pt$ requires C, 24·65; H, 2·5%). It is slightly more soluble than its chloro-analogue.

*Reaction between Di*cyclo*pentadienedichloroplatinum and Sodium Thiocyanate.*—The chloro-complex (0·3 g.) and sodium thiocyanate (0·24 g.) in acetone (20 c.c.) were boiled for a few minutes, to give a pale yellow solution from which sodium chloride soon separated. The solution was cooled, filtered, and taken to dryness at 15 mm. The residue, washed with water and dried, was purified by reprecipitation from a large amount of chloroform by diethyl ether, and so obtained in very small white needles (0·2 g.), decomp. 200—205° (Found: C, 32·75; H, 2·75; N, 6·3. $C_{12}H_{12}N_2S_2Pt$ requires C, 32·5; H, 2·7; N, 6·3%). The *dithiocyanate* is sparingly soluble in boiling acetone, chloroform, and benzene, and is decomposed by boiling methylene chloride.

cyclo*Octa*-1 : 5-*dienedichloroplatinum*, $[C_8H_{12}PtCl_2]$, was prepared in the same way as its di*cyclo*pentadiene analogue from sodium chloroplatinite hydrate (4·0 g.) and *cyclo*octadiene (4·0 c.c.) and crystallised from acetic acid (charcoal) in white needles, decomp. 220—278° (1·9 g.) (Found: C, 25·55; H, 3·2. $C_8H_{12}Cl_2Pt$ requires C, 25·7; H, 3·2%), insoluble in most organic solvents except boiling chloroform, methylene chloride, and acetic acid. The same product is obtained but more slowly by the reaction between sodium chloroplatinate and *cyclo*octadiene in ethanol.

cyclo*Octa*-1 : 5-*dienedibromoplatinum*, $[C_8H_{12}PtBr_2]$, was prepared in good yield from hydrated sodium chloroplatinite, diene, and lithium bromide in the same way as its di*cyclo*pentadiene analogue, but in ethanol. It recrystallised from acetic acid in pale yellow needles, decomp. 200—270° (Found: C, 20·6; H, 2·6. $C_8H_{12}Br_2Pt$ requires C, 20·7; H, 2·6%), slightly more soluble than its chloro-analogue in organic solvents.

cyclo*Octa*-1 : 5-*dienedi-iodoplatinum*, $[C_8H_{12}PtI_2]$, was prepared analogously to the corresponding bromide. It crystallised from acetic acid in orange-yellow needles contaminated with some brown crystalline by-product. Precipitation from boiling methylene chloride by light petroleum (b. p. 40—60°) gave an orange-yellow powder, decomp. about 250° (Found: C, 17·4; H, 2·2. $C_8H_{12}I_2Pt$ requires C, 17·25; H, 2·2%).

Dipentenedichloroplatinum, $[C_{10}H_{16}PtCl_2]$, was prepared and purified in the same way as its di*cyclo*pentadiene analogue (chloroplatinite, 4 g., and pure dipentene, 2·2 c.c., in propanol, 80 c.c., gave 1·5 g. of cream-coloured needles). This product has the same infrared spectrum as that product prepared by Chatt and Wilkins's method [3] and described as the β-isomer. In methanol instead of propanol, this reaction requires 5 days.

Hexa-1 : 5-dienedichloroplatinum, $[C_6H_{10}PtCl_2]$, was obtained from the chloroplatinite (2 g.) and diene (2·5 c.c.) in propanol (60 c.c.) but only in poor yield (0·4 g.) The main product was $Na_2[C_6H_{10}(PtCl_3)_2]$.

*Bis(di*cyclo*pentadiene Methoxide)-μμ'-dichlorodiplatinum*,* $[(C_{10}H_{12}OMe)_2Pt_2Cl_2]$.—Di*cyclo*pentadienedichloroplatinum (0·4 g.), suspended in methanol (25 c.c.), was heated to boiling and sodium acetate (approx. 0·2 g.) added. The solids dissolved and on continued heating a white solid was precipitated. After cooling, the solid was filtered off, washed with methanol, and dried. Recrystallisation was effected by diluting a solution in chloroform with ether (yield 0·3 g.) (Found: C, 33·7; H, 3·9; OMe, 7·9%; *M*, ebullioscopic in 1·1% chloroform solution, 726. Calc. for $C_{22}H_{30}O_2Cl_2Pt_2$: C, 33·55; H, 3·8; Pt, 49·5; OMe, 7·9%; *M*, 788). It is a non-electrolyte in nitrobenzene solution. This compound is identical (infrared spectra) with

* Trivial names of this type have been adopted when it is not known which double bond has been destroyed and when systematic names would be very involved.

a sample obtained by Hofmann and von Narbutt's method [6] (Found: C, 33·2; H, 3·9; Pt, 49·15; OMe, 7·9%). It can also be obtained as follows:

(*a*) The dichloro-derivative (0·3 g.) was suspended in boiling methanol (20 c.c.), and a small amount of anhydrous sodium carbonate added. The chloro-compound dissolved and the solution was filtered. The methoxy-chloride separated from the filtrate as it cooled (yield, pure, 0·24 g.).

(*b*) The dichloro-derivative (0·4 g.) was suspended in cold methanol (8 c.c.), and sodium methoxide from metallic sodium (0·025 g.) and methanol (5 c.c.) was added. After a few minutes the solid had changed in appearance and the solution was neutral. The solid was filtered off, washed with methanol, and dried (yield, 0·13 g.) (Found: C, 33·6; H, 3·8%).

Bis(dicyclopentadiene Methoxide)-μμ'-di-iododiplatinum, $[(C_{10}H_{12}OMe)_2Pt_2I_2]$.—The corresponding chloride (0·35 g.), boiled for a few minutes with lithium iodide (*ca.* 4 mols.) in acetone (15—20 c.c.), gave a pale yellow solution which was filtered and diluted with methanol. On cooling, the *product* (0·32 g.) separated and was purified in the same way as its chloro-analogue (Found: C, 27·0; H, 3·2. $C_{22}H_{30}O_2I_2Pt_2$ requires C, 27·2; H, 3·1%); it is slightly more soluble in organic solvents than its chloro-analogue.

The iodo-compound (0·27 g.) in chloroform (25 c.c.) was treated with *p*-toluidine (0·046 g.); there was no apparent colour change; the solution was boiled for 2 min. and then taken to dryness at 15 mm.; 0·16 g. of the iodo-starting material was recovered (identified by infrared spectrum).

Bis(dicyclopentadiene Methoxide)-μμ'-dithiocyanatodiplatinum, $[(C_{10}H_{12}OMe)_2Pt_2(SCN)_2]$.—A methanol (*ca.* 15 c.c.) suspension of the methoxy-chloride (0·3 g.) and sodium thiocyanate (approx. 0·2 g.) was boiled for a few minutes. The starting material did not dissolve but changed in appearance. After cooling, the mixture was filtered, and the residual *product* washed with water, dried, and purified in similar manner to the methoxy-chloride (yield, 0·12 g.) (Found: C, 34·6; H, 3·6; N, 3·5. $C_{24}H_{30}O_2N_2S_2Pt_2$ requires C, 34·6; H, 3·6; N, 3·4%). It is sparingly soluble in boiling chloroform, acetone, and benzene.

Bis(dicyclopentadiene Methoxide)-μμ'-di(ethylthio)diplatinum, $[(C_{10}H_{12}OMe)_2Pt_2(SEt)_2]$.—A solution of sodium ethyl sulphide (1·5 c.c. of a solution containing 0·5 c.c. of ethanethiol and 0·16 g. of sodium in 10 c.c. of methanol) was added to a suspension of the methoxy-chloride (0·4 g.) in methanol (25 c.c.). The mixture was warmed slightly for a few minutes, and the resulting pale yellow solution taken to dryness at 15 mm. The residual solid was extracted with chloroform and the *product* obtained as an oil by the evaporation of the extract at 15 mm. The oil crystallised on contact with hot methanol, from which it was recrystallised (yield 0·16 g.) (Found: C, 37·5; H, 4·9; S, 7·3. $C_{26}H_{40}O_2S_2Pt_2$ requires C, 37·2; H, 4·8; S, 7·65%). It is a non-electrolyte in nitrobenzene. It is very soluble in chloroform and benzene and moderately so in acetone, ether, boiling methanol, or light petroleum.

(*Dicyclopentadiene Methoxide*)-p-*toluidinechloroplatinum*, $[C_{10}H_{12}OMe,p\text{-toluidinePtCl}]$.—*p*-Toluidine (0·107 g.) was added to the methoxy-chloride (0·4 g.) in chloroform, and the solution taken to dryness at 15 mm. The residual *product* recrystallised from methanol (yield 0·4 g.) (Found: C, 43·0; H, 4·8; N, 3·15; Pt, 38·7%; *M*, ebullioscopic in 1·5% benzene solution, 526. $C_{18}H_{24}ONClPt$ requires C, 43·15; H, 4·8; N, 2·8; Pt, 38·9%; *M*, 501). It is a non-electrolyte in acetone; it is very soluble in cold chloroform, moderately so in benzene, methanol, acetone, and ether, and insoluble in nitrobenzene.

From methanol (10 c.c.) solution of $[C_{10}H_{12}OMe,p\text{-toluidinePtCl}]$ (0·1 g.) and lithium iodide (*ca.* 0·05 g.), boiled for 2 min., pale yellow $[(C_{10}H_{12}OMe)_2Pt_2I_2]$, decomp. 192—215° (0·07 g.; identified by its infrared spectrum), was recovered.

Bis(dicyclopentadiene ethoxide)-μμ'-dichlorodiplatinum, $[(C_{10}H_{12}OEt)_2Pt_2Cl_2]$, was prepared and purified analogously to the methoxy-chloride by using ethanol and sodium carbonate (yield 0·23 g. from 0·3 g. of dichloride) (Found: C, 35·5; H, 4·2%; *M*, ebullioscopic in 1·9% benzene solution, 858. Calc. for $C_{24}H_{34}O_2Cl_2Pt_2$: C, 35·3; H, 4·2%; *M*, 816).

It was also prepared by using the stoicheiometric amount of sodium ethoxide (0·07 g. from 0·4 g. of dichloride), but decomposition products were also formed.

We attempted to prepare it as described by Hofmann and von Narbutt,[6] at 40° and at room temperature, but obtained only the dichloro-complex $[C_{10}H_{12}PtCl_2]$.

Bis(dicyclopentadiene n-*Propoxide)-μμ'-dichlorodiplatinum* $[(C_{10}H_{12}OPr^n)_2Pt_2Cl_2]$.—A small amount of anhydrous sodium carbonate was added to a solution of hydrated sodium chloroplatinite (2 g.) in propan-1-ol (35 c.c.) containing dicyclopentadiene (3 c.c.), and the mixture

kept at room temperature for 5 days. The white crystalline *product* was filtered off, washed with ether and water, and dried (yield, 1·90 g.). It was then practically pure, but can be purified further by dissolving it in boiling chloroform and reprecipitating it with ether (Found: C, 37·1; H, 4·7. $C_{16}H_{28}O_2Cl_2Pt_2$ requires C, 37·0; H, 4·5%). It is soluble in cold chloroform and hot benzene, moderately so in acetone, and insoluble in propanol, ether, and light petroleum. It was also obtained from the dichloride by the sodium carbonate method, but then contained a small amount of impurity which was not eliminated by recrystallisation. The presence of the impurity was confirmed by comparing the infrared spectra of the two samples.

Bis-(8-methoxycyclooct-4-enyl)-μμ'-dichlorodiplatinum, $[(C_8H_{13}OMe)_2Pt_2Cl_2]$.—Finely powdered *cyclo*octa-1 : 5-dienedichloroplatinum (1·4 g.) and anhydrous sodium carbonate were boiled in methanol (70 c.c.) for a few minutes and the hot solution filtered. Cooling the filtrate to room temperature gave white needles but keeping it at −70° for 3 days gave a white microcrystalline powder which was filtered off and dried. This, the required *product*, was purified by reprecipitation from chloroform with ether (yield, 0·81 g.) (Found: C, 29·1; H, 4·2. $C_{18}H_{30}O_2Cl_2Pt_2$ requires C, 29·2; H, 4·1%). It is slightly more soluble than its di*cyclo*pentadiene analogue in organic solvents.

Bis-(8-methoxycyclooct-4-enyl)-μμ'-di-iododiplatinum, $[(C_8H_{13}OMe)_2Pt_2I_2]$.—*cyclo*Octa-1 : 5-dienedi-iodoplatinum (0·5 g.) and a small amount of anhydrous sodium carbonate were boiled in methanol (25 c.c.) for a few minutes. The di-iodide dissolved and the hot solution was filtered. On evaporation at 15 mm. pressure, the crude *product* was obtained as a brown solid. It was purified by precipitating it thrice from chloroform with ether (yield 0·2 g.) (Found: C, 23·8; H, 3·4. $C_{16}H_{28}O_2I_2Pt_2$ requires C, 23·4; H, 3·3%).

8-Methoxycyclooct-4-enyl-p-toluidinechloroplatinum, $[C_8H_{13}OMe,p\text{-toluidine,PtCl}]$.—*p*-Toluidine (0·093 g.) was added to the methoxy-chloride (0·32 g.) in chloroform (10 c.c.), and the resulting solution taken to dryness at 15 mm. The product remained as a solid which was purified by repeated precipitation from benzene by ligroin (yield, 0·34 g.). A better *product* is obtained, but wastefully, by recrystallisation from methanol (Found: C, 40·6; H, 5·0; N, 3·35. $C_{16}H_{24}ONClPt$ requires C, 40·3; H, 5·1; N, 2·9%). It is a non-electrolyte in nitrobenzene.

Bis(dipentene Methoxide)-μμ'-dichlorodiplatinum, $[(C_{10}H_{16}OMe)_2Pt_2Cl_2]$.—A methanol (40 c.c.) suspension of dipentenedichloroplatinum (1 g.) and a small amount of anhydrous sodium carbonate was boiled for a few minutes. The dichloride dissolved, giving a light brown solution which was filtered and kept at −70° for 3 days. The solid which had separated was filtered off and purified by precipitation from chloroform with ether (yield 0·1 g.) (Found: C, 33·4; H, 4·9. $C_{22}H_{38}O_2Cl_2Pt_2$ requires C, 33·2; H, 4·8%). It is the least stable and most soluble of the methoxy-chlorides obtained.

Dimethoxy- and Dihydroxy-derivatives of $[C_8H_{12}PtCl_2]$.—The " α-dimethoxide " was obtained as a solid by evaporating to dryness the methanol reaction mixture from which the $[(C_8H_{12}OMe)_2Pt_2Cl_2]$ had been filtered {see preparation of $[(C_8H_{12}OMe)_2Pt_2Cl_2]$}. (Yield, pure, 0·1 g.) Also it is the primary product which separates in white needles on first cooling the reaction mixture to room temperature. (0·4 g. from 0·7 g. of dichloride). When purified by reprecipitating it from chloroform with methanol, it decomposed at 140—150° (Found: C, 33·1; H, 5·1; Pt, 53·25%; *M*, ebullioscopic in 2·1% benzene solution, *ca.* 1150. $C_{10}H_{18}O_2Pt$ requires C, 32·9; H, 5·0; Pt, 53·4%; *M*, 365). It is probably a polymeric dimethoxide $[C_8H_{12}Pt(OMe)_2]_n$ ($n \sim 3$ or 4). It is very soluble in chloroform, hot methanol and hot benzene, slightly soluble in ether, and insoluble in light petroleum.

The " dihydroxide " was obtained when sodium chloroplatinite tetrahydrate (4 g.) and *cyclo*octa-1 : 5-diene (*ca.* 4 c.c.) in methanol (40 c.c.) with the addition of a little anhydrous sodium carbonate were kept for 3 days. The crystalline *product* (1·7 g.) was filtered off, washed with methanol and then water, and dried. Recrystallised twice from much acetic acid it was obtained in white needles, decomp. 190—210° (0·8 g.) (Found: C, 28·5; H, 4·0; Pt, 57·1. $C_8H_{14}O_2Pt$ requires C, 28·5; H, 4·2; Pt, 57·8%). It is a non-electrolyte in nitrobenzene and only sparingly soluble in most organic solvents. The " β-dimethoxide " was obtained when a methanol (45 c.c.) solution of the dihydroxide (0·54 g.) was boiled for a few minutes with a little anhydrous sodium carbonate and the hot solution was filtered. The *product* separated as the filtrate cooled. A further quantity was obtained by extracting the residue from the filtration with cold chloroform (20 c.c.) and diluting the extract with methanol (30 c.c.). Purified by reprecipitation from chloroform with methanol, it was obtained in white plates,

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decomp. 140—160°, slowly becoming cream-coloured (Found: C, 32·2; H, 4·8%). It is less soluble in methanol than the "α-dimethoxide" and has a different infrared spectrum.

The compounds were finely ground and suspended in "Nujol" for examination of their infrared spectra, which were measured with a Grubb-Parsons S3A spectrometer with a rock-salt prism.

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487. *Fluorocyclohexanes. Part I.* cis- *and* trans-1H : 2H-*Decafluorocyclohexanes.*

By R. P. SMITH and J. C. TATLOW.

Improved conditions are described for the preparation of polyfluoro*cyclo*hexanes [1, 2] by the treatment of benzene with cobaltic fluoride at 150—200°. The investigations were considerably simplified by application of gas chromatography. Besides the undeca- and deca-fluoro*cyclo*hexanes described before,[2-4] a fraction, b. p. 70°, has been isolated and identified, after dehydrofluorination studies, as *trans*-1*H* : 2*H*-decafluoro*cyclo*hexane (I). Re-examination of an alternative synthesis of 1*H* : 2*H*-decafluoro*cyclo*hexane showed that the product, b. p. 91°, obtained before [5] was the *cis*-isomer (II), but that a small proportion of the *trans*-compound was formed as well. These allocations of structure have been confirmed by measurements of dipole moments.

EARLIER studies [1, 2] have dealt with the production of polyfluoro*cyclo*hexanes by the fluorination of benzene, in the vapour phase, with cobaltic fluoride at about 150°. In this paper we describe improvements in the preparation of these polyfluorides, including the application of gas chromatography [4, 6] to the detection and isolation of the individual compounds. Also, a further component of the mixture, a 1*H* : 2*H*-decafluoro*cyclo*hexane (I), has been identified. Since another compound (II) having this basic structure had been reported from an alternative synthesis,[5] investigations of the stereochemistry of these highly fluorinated *cyclo*hexanes have now been initiated.

*Preparation and Isolation of the Polyfluoro*cyclo*hexanes.*—For the fluorination of benzene a copper reaction vessel, incorporating a stirrer and based on an earlier design,[7] was used, and gave consistently good yields. As before, for the isolation of pure components, nearly all of which are low-melting solids, fractional distillation was employed. Much trouble had been experienced previously in removing the relatively small proportion of perfluoro*cyclo*hexane, which, having no liquid range, sublimed and blocked the fractionating equipment. This was overcome by addition of diethyl ether which forms an azeotrope with perfluoro*cyclo*hexane but not with fluorohydrocarbons present. The two chief products

[1] Barbour, Mackenzie, Stacey, and Tatlow, *J. Appl. Chem.*, 1954, **4**, 341.
[2] *Idem*, *ibid.*, p. 347.
[3] Evans and Tatlow, *J.*, 1954, 3779.
[4] *Idem*, (*a*) *J.*, 1955, 1184; (*b*) "Vapour Phase Chromatography" (ed. Desty), Butterworths, London, 1956, p. 256.
[5] Roylance, Tatlow, and Worthington, *J.*, 1954, 4426.
[6] James and Martin, *Biochem. J.*, 1952, **50**, 679; *Analyst*, 1952, **77**, 915.
[7] Barbour, Barlow, and Tatlow, *J. Appl. Chem.*, 1952, **2**, 127.

in the lower boiling range, as before, were undeca- and deca-fluoro*cyclo*hexane (b. p. 78°), but an inflexion at about 70° in the distillation curves prompted refractionation of intermediates, which gave a new product (I). At this point in the investigation, gas chromatography became available [6, 4] and considerably simplified the separation of the complex polyfluoro*cyclo*hexane mixture. Preliminary analytical gas chromatography showed at least ten components (see Table). Fractional distillations of this product (2—3 kg., through 4′ columns) were then controlled by analytical chromatography, which improved the efficiency since the purity of fractions was assessed as they were being collected. Most of the major components of the mixture were obtained reasonably pure in this way.[4b, 8]

Characterisation of the 1H : 2H-*Decafluoro*cyclo*hexanes.*—Elemental analysis showed that the new polyfluoride (I) (b. p. 70°) was a decafluoro*cyclo*hexane. It was unusually resistant to aqueous potassium hydroxide : under conditions by which undecafluoro*cyclo*hexane was converted completely into perfluoro*cyclo*hexene, less than half of the new decafluoride had been attacked, as was shown by the liberation of fluoride ion. Analytical gas chromatography of the product showed four peaks, coincident with those given by perfluoro*cyclo*hexa-1 : 3-diene [3] (III), 1*H*-nonafluoro*cyclo*hex-1-ene [5] (IV), the starting material (I), and 3*H*-nonafluoro*cyclo*hex-1-ene [4] (a very small peak only was given by this component). A second treatment with alkali removed the starting material (I) and the trace of 3*H*-olefin, leaving the 1 : 3-diene (III) and the 1*H*-ene (IV). The isolation of pure specimens of these olefins (they have very similar properties and almost identical boiling points) could be accomplished only by preparative-scale gas chromatography.[4] Even with this technique it was necessary to use favourable conditions (low column temperature, small initial charge of the mixture) to effect a clean separation. The diene sample (*ca.* 16% of the product) was characterised by gas chromatography and infrared spectroscopy. The mono-olefin (IV) (80% of the product) was identified chromatographically, by its infrared spectrum, and by oxidation to octafluoroadipic acid. The very small amount of 3*H*-nonafluoro*cyclo*hex-1-ene present was only detected chromatographically; 4*H*-nonafluoro*cyclo*hex-1-ene [4] was never detected in these investigations.

The formation by dehydrofluorination of the olefins (III) and (IV) and the complete

*Gas chromatography of the polyfluoro*cyclo*hexane mixture.*

No. of peak	1	2	3	4	5	6
Retention time (min.)	2·2	5·1	6·6	7·5	12·9	16·6
Relative peak area *	m	l	—	m	l	m
Compound	C_6H_{12}	C_6HF_{11}	Et_2O	*trans*-1*H* : 2*H*	Mixed †	1*H* : 4*H* †
					$C_6H_2F_{10}$	
B. p.	—	63°	34°	70°	78°	86°

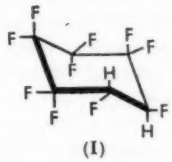
No. of peak	7	8	9	10	11	12
Retention time (min.)	20·0	25·6	33·4	45·0	50·0	53·0
Relative peak area *	l	s	s	m	s	m
Compound	$C_6H_3F_9$ †	$C_6H_2F_{10}$ †	$C_6H_2F_{10}$ †	Not yet identified		
B. p.	92°	91°	89°	—	—	—

* l = large, m = medium, s = small. † To be reported later.

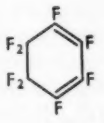
absence from the products of 4*H*-nonafluoro*cyclo*hex-1-ene clearly established that the new decafluoride (I) (b. p. 70°) possessed a 1*H* : 2*H*-structure. However, a different compound (II) (b. p. 91°) having this basic structure had been made earlier,[5] by an unequivocal synthesis involving the photochemical addition of chlorine to decafluoro*cyclo*hexene, and then replacement of the chlorine by hydrogen by means of lithium aluminium hydride. Accordingly, this work [5] was repeated, and analytical chromatography of the product revealed the presence, not only of the high-boiling form (II) as the major component, but also of the new isomer (I) in smaller amounts, not detected previously. Both compounds were isolated by preparative-scale chromatography, and characterised completely. The

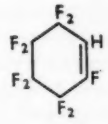
[8] Godsell, Stacey, and Tatlow, *Nature*, 1956, **178**, 199, and unpublished work.

dehydrofluorination of the two isomers (I) and (II) was repeated. The two samples of the more volatile compound (I), isolated from the polyfluoro*cyclo*hexane mixture and from the reduction product of the 1 : 2-dichloride, gave an identical gas-chromatographic trace. This showed the presence of the 1 : 3-diene (III), the 1*H*-mono-ene (IV), and the starting material. In confirmation of the earlier work,[5] the higher-boiling decafluoride (II), under similar conditions, gave only the 1*H*-ene (IV), with no starting material. A very small step on the leading edge of the peak given when the chromatographic tube was overloaded with this sample of the olefin (IV) may have been due, however, to the presence of a trace of the diene (III).


(I)

(II)


(III)


(IV)

Stereoisomerism of the 1H : 2H-*Decafluoro*cyclo*hexanes.*—There are two stereoisomers of a 1 : 2-disubstituted *cyclo*hexane,[9, 10, 11] of which, for convenience, these decafluoro*cyclo*hexanes may be considered examples, though of course the two hydrogen " substituents " are smaller than the fluorine atoms. The *cis*-form has one axial and one equatorial hydrogen atom in both possible conformations. These are mirror images of each other, but, presumably, resolution of the optical isomers is impossible. The *trans*-form, in one conformation, has both hydrogen atoms in axial positions, whilst in the other, both are equatorial. In this case, each conformation can exist in mirror-image forms, and resolution of these optical isomers should theoretically be possible, since they are not interconvertible. Experimentally, neither stereoisomer (I) or (II) was optically active; the *trans*-form should of course be synthesised as a racemate. No ready means of resolving fluorohydrocarbon racemates is available at present.

As a mechanism [12] by which dehydrohalogenations of *cyclo*hexane derivatives proceed, the preferred process is generally considered to be a concerted bimolecular one (E_2), in which the eliminated groups, hydrogen and halogen, are originally *trans* to each other, *i.e.*, occupy axial positions. For the all-*cis*-structure " β-benzene hexachloride," the slow bimolecular dehydrochlorination is thought [13, 14] to proceed *via* a carbanion intermediate. Another possible mechanism, the two-stage unimolecular elimination (E_1), has not been established for alkaline dehydrochlorinations. Dehydrohalogenations of 1 : 1- and 1 : 2-dihalogeno*cyclo*hexanes by aqueous-alcoholic sodium hydroxide have been studied recently.[15] The 1 : 1- and *cis*-1 : 2-dihalides gave exclusively the analogous 1-halogeno*cyclo*hex-1-ene with elimination of 1 mol. of hydrogen halide by the concerted mechanism (E_2). The *trans*-1 : 2-dihalides eliminated 2 mol. of hydrogen halide to give exclusively *cyclo*hexa-1 : 3-diene in a slow bimolecular reaction (no *cis*-elimination occurred). The influence of conformation is very striking here. Dehydrochlorination [16] of *trans*-1 : 2-dichloro*cyclo*hexane with quinoline, however, gave approximately equimolar amounts of 1-chloro-*cyclo*hex-1-ene (*cis*-elimination) and the 1 : 3-diene (*trans*-elimination).

On the assumption that these mechanisms applied also to polyfluoro*cyclo*hexanes, the relative ease of dehydrofluorination of the higher-boiling decafluoride (II) suggested

[9] (*a*) Hassel, *Quart. Rev.*, 1953, **7**, 221; (*b*) Barton and Cookson, *ibid.*, 1956, **10**, 44.
[10] Orloff, *Chem. Rev.*, 1954, **54**, 347.
[11] Riemschneider and Geschke, *Angew. Chem.*, 1953, 390.
[12] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 419.
[13] Cristol, *J. Amer. Chem. Soc.*, 1947, **69**, 338; Cristol, Hause, and Meek, *ibid.*, 1951, **73**, 674.
[14] Orloff and Kolka, *ibid.*, 1954, **76**, 5484.
[15] Goering and Espy, *ibid.*, 1956, **78**, 1454.
[16] Stevens and Grummitt, *ibid.*, 1952, **74**, 4876.

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that it was the *cis*-isomer. The possession of one axial and one equatorial hydrogen atom ensured that a hydrogen and a fluorine atom of the $-CHF\cdot CHF-$ system were always axial, so that loss of hydrogen fluoride could occur by the orthodox process (E_2) to give the mono-olefin. Since the stability of carbon–fluorine bonds is greater in CF_3 and CF_2 than in CHF groups, the experimental loss of fluorine from position 2 rather than from position 6 is readily understandable.

The lower-boiling decafluoride (I) was much more resistant to dehydrofluorination than its isomer (II), and gave a mixture of the monolefin (IV) and the conjugated diolefin (III). This also is in accord with the expected stereochemical requirements, since the *trans*-isomer, with both hydrogen atoms axial or both equatorial, cannot exist in a form which would allow *trans*-elimination of hydrogen fluoride from the $-CHF\cdot CHF-$ system ($C_{(1)}$ and $C_{(2)}$). The favoured conformation of the *trans*-isomer should be that with the small hydrogen atoms arranged axially, and then dehydrofluorination could proceed either by a *cis*-elimination of hydrogen fluoride from $C_{(1)}$ and $C_{(2)}$ to give the olefin (IV) or by a two-fold *trans*-elimination ($C_{(1)}$ and $C_{(6)}$, $C_{(2)}$ and $C_{(3)}$) to give the diene (III). The first reaction would be favoured electronically (because of the increased stability of fluorine in CF_2 compared with CHF); the second would be favoured stereochemically. In practice, the electronically favoured *cis*-elimination appears to predominate. *cis*-Eliminations from *trans*-substituted toluene-*p*-sulphonyl esters of *cyclo*hexane derivatives have been reported;[17] the acidity increase of the hydrogen here overshadows the stereochemical effect. Qualitatively, the dehydrofluorination of the *trans*-1*H* : 2*H*-decafluoride (I) is slower than that of undecafluoro*cyclo*hexane, though here also the fluorine is lost from a CF_2 group. The greater acidity of a hydrogen atom flanked by two CF_2 groups, compared with one flanked by CF_2 and CHF, may explain this effect.

These allocations of structure were tested by measurements of the dipole moments of the two 1*H* : 2*H*-decafluorides, those of undecafluoro*cyclo*hexane and perfluoro*cyclo*hexane being measured also for comparison. Results were : C_6F_{12}, 0; C_6HF_{11}, **1·64**; $C_6H_2F_{10}$ (b. p. 91°), 2·59; $C_6H_2F_{10}$ (b. p. 70°), 0·88. The value for the isolated C–H dipole in a polyfluoride agrees well with those reported recently for fluoroform [18] (1·62), pentafluoroethane [18] (1·54), and for 1*H*-heptafluoropropane [19] (1·62 ± 0·12). The expected dipole moment of the two equivalent *cis*-structures (1*H* a : 2*H* e and 1*H* e : 2*H* a), calculated from that of the undecafluoride, is 2·69. This is in reasonable agreement, considering the approximations inherent in the determinations, with the experimental value (2·59) found for the isomer of b. p. 91° (II). In the case of the isomer of b. p. 70° (I), the experimental value (0·88) of the dipole moment is sufficiently low to show that this compound must have the *trans*-structure, and that the conformation with the two axial hydrogen atoms predominates. The 1*H* e : 2*H* e conformation of the structure would have a dipole moment very similar (calculated value 2·69) to that of the *cis*-isomer, whereas the 1*H* a : 2*H* a conformation is the only 1*H* : 2*H*-system that should have a very low moment. The experimental value may result (i) from small experimental errors, (ii) from the small dipole inherent in a system with two diaxial hydrogen atoms (the so-called inductive effect), (iii) from the presence of some of the conformation with two equatorial hydrogens, or from a combination of these factors. Because of this uncertainty, it would not seem justifiable to calculate the ratio of the numbers of molecules in each conformation, or the energy difference between the two forms. Suffice it that calculations directly from the experimental dipole moment show that apparently in not more than about 10% of the molecules are the hydrogen atoms equatorial; probably the proportion is less than this.

Thus, all the evidence so far available, both chemical and physical, indicates that the two products obtained are *trans*-(1*H* a : 2*H* a) (I), b. p. 70°, and *cis*-1*H* : 2*H*-decafluoro-*cyclo*hexane (1*H* a : 2*H* e) (II), b. p. 91°. It is of interest that the latter isomer, which

[17] Bordwell and Kern, *J. Amer. Chem. Soc.*, 1955, **77**, 1141.
[18] Di Giacomo and Smyth, *ibid.*, p. 774.
[19] Rogers and Pruett, *ibid.*, p. 3686.

should be less favoured sterically, is the main product from the synthesis involving photochemical addition of chlorine to perfluoro*cyclo*hexene followed by reduction with lithium aluminium hydride. If the latter stage proceeds with retention or inversion of configuration, as seems probable, then a predominantly *cis*-addition of chlorine is indicated (*cis*- as well as *trans*-additions of chlorine to tetrachloro*cyclo*hexenes have been reported [20]). In the case of perfluoro*cyclo*hexene, after the first attack by a chlorine atom, the chlorine substituent (being larger than fluorine) should take up an equatorial position. On the adjacent carbon, if the intermediate radical can rearrange so that the fluorine substituent here becomes essentially equatorial, the *cis*-adduct would be obtained as the final product (cf. a rather similar postulate for intermediate carbonium anions [9b]).

Though fluoro*cyclo*hexanes have been investigated very little as yet, much is now known about the important and related chloro*cyclo*hexane series.[10, 21] Dipole-moment measurements have been made [22] on the 1 : 2-dihalogeno*cyclo*hexanes with results which indicate that the favoured conformations of the *trans*-compounds are not as for our decafluorides, owing in part to the different sizes of the substituents. Some of the many dehydrochlorination studies reported have been mentioned above. The great strength of the C–F bond and the relatively small size of the fluorine atom together make the fluoro*cyclo*hexanes a unique and interesting group. From the polyfluoro*cyclo*hexane mixture obtained from benzene, the other four decafluoro- and two nonafluoro-*cyclo*hexanes have now been isolated and characterised [23] and will be described later.

Experimental

Fluorination Apparatus.—This was based on those described earlier.[7] The chief differences were as follows: the body was of copper tube (3 ft. 6 in. long; $3\frac{7}{8}$ in. internal diam.; $\frac{3}{16}$ in. wall thickness), and the two bearings of the stirrer shaft were simplified. Each comprised a plain bearing (carrying the shaft) adjacent to which was a "Fluon" bush in which the shaft ran. These bushes were compressed into their housings by strong springs, and made efficient self-lubricating gas-tight seals with which no nitrogen-sweep or water-cooling was necessary if the reaction-vessel temperatures did not exceed about 250°. The vessel was charged as before with 3·5 kg. of cobaltic fluoride. The seven heaters were of an improved design, the elements being carried in firebricks (HT 1 Refractory) hollowed out to fit around the tube, and into which slots had been cut. The other features and the ancilliary equipment were as described earlier.

*Production of Polyfluoro*cyclo*hexanes from Benzene.—Fluorination.* Benzene (65·5 g.) was introduced into the reaction vessel at a steady rate from a dropper during 3 hr. The vessel temperature was initially approx. 170°, along its length, and as the reaction proceeded the heat of reaction gave rise to an increase of 30—50° which passed along the reaction vessel as a narrow "hot zone." No attempt was made to compensate for this increase (somewhat improved yields would have resulted, but at the expense of constant attention: the conditions described required little attention). The apparatus was then swept out with a slow stream of nitrogen for *ca.* $\frac{1}{2}$ hr. and the trap was warmed to about 20° and the contents were poured into water. The semi-solid product was washed with water until free from hydrogen fluoride, most of the water was decanted, the product was allowed to solidify (cooled below 15°), and the rest of the water was then poured off. The polyfluoride mixture (180 g.) was a white wax, virtually free from benzene (which forms azeotropes with the lower-boiling fluorides).

The cobaltic fluoride in the reaction vessel was regenerated by passage at about 170° of fluorine (*ca.* 250 g.) during 15 hr. After being swept out with nitrogen the vessel was ready for further use.

Distillation. To the product (1629 g.) from nine such runs, ether (150 c.c.) was added, and

[20] Kolka, Orloff, and Griffing, *J. Amer. Chem. Soc.*, 1954, **76**, 3940.
[21] Metcalf, "Organic Insecticides," Interscience Publ. Inc., New York, 1955, p. 213.
[22] Tulinskie, Di Giacomo, and Smyth, *J. Amer. Chem. Soc.*, 1953, **75**, 3552; Kozima, Sakashita, and Maeda, *ibid.*, 1954, **76**, 1965; Bender, Flowers, and Goering, *ibid.*, 1955, **77**, 3463; Kwestroo, Meijer, and Havinga, *Rec. Trav. chim.*, 1954, **73**, 717.
[23] Evans, Godsell, Stephens, and Tatlow, unpublished work.

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the solution was washed with aqueous sodium carbonate, then with water, separated, and fractionally distilled, from phosphoric oxide, through a 2′ column packed with gauze spirals. Fractions obtained were : the azeotrope of ether and perfluoro*cyclo*hexane, b. p. 27·5°; a small excess of ether, b. p. 34° (when the temperature rose above 27·5°, more ether was added until it no longer fell to 27·5°; an excess of ether was then present); undecafluoro*cyclo*hexane (345 g.), b. p. 63—64°; intermediate fraction (110 g.), b. p. 64—77° (an inflexion occurred at 70° in the distillation curve); decafluoro*cyclo*hexane (185 g.), b. p. 77·5—79°; still residue (700 g.) (solid when cold).

Refluorination. To still residues, b. p. >80°, similar to that mentioned above (3500 g.), benzene (305 g.) was added, to give a liquid mixture. This was fluorinated, as described before, in 11 batches, at reaction temperatures of about 190°, there being very little heat of reaction. After isolation as described before, the product (2600 g.) was mixed with a little ether and fractionated. After removal of the azeotrope, undecafluoro*cyclo*hexane (670 g.), b. p. 63·4—63·7°, and decafluoro*cyclo*hexane (250 g.), b. p. 78—79°, were obtained with no evidence of a flat part in the distillation curve corresponding to the compound, b. p. 70°.

Application of gas chromatography. The crude polyfluoro*cyclo*hexane mixture was liquefied with a little ether, the mixture (0·01 c.c.) was put through a 6′ chromatography column, packed with dinonyl phthalate–kieselguhr (1 : 2), at 100° (nitrogen flow rate 0·45 l./hr.) with the result shown in the Table. The peak given by compound (8) is coincident with that from authentic *cis*-1*H* : 2*H*-decafluoro*cyclo*hexane, and the boiling point also is identical. The later peaks may well be incompletely resolved. Some material was retained even longer than 60 min., but gave only broad ill-defined peaks under these conditions.

Isolation of the Polyfluoride having b. p. 70°.—Intermediate fractions (590 g.), b. p. 64—77°, from various series of fluorinations, were fractionally distilled through a 2′ column. There was obtained, after the removal of undecafluoro*cyclo*hexane, trans-1H : 2H-*decafluoro*cyclo*hexane* (150 g.), b. p. 70·0—71·0°, m. p. 20·5—21·5°, n_D^{25} 1·2929 (Found : C, 27·1; H, 0·8; F, 71·6. $C_6H_2F_{10}$ requires C, 27·3; H, 0·8; F, 71·9%).

Subsequently, gas chromatography of this product (dinonyl phthalate–kieselguhr 1 : 2, temp. 78°, nitrogen flow rate 1·2 l./hr.) showed, by overloading of the tube, the presence of traces of undecafluoro*cyclo*hexane and of decafluoro*cyclo*hexane (b. p. 78°). For the later stages of the examination detailed below, the material was purified by passage through the preparative-scale gas-chromatographic column.[4]

Dehydrofluorination of trans-1H : 2H-*Decafluoro*cyclo*hexane.—Analytical-scale work. trans*-1*H* : 2*H*-Decafluoro*cyclo*hexane (2·64 g.) was refluxed for 6 hr. with potassium hydroxide (10 g.) and water (10 c.c.) in a flask with a condenser cooled by solid carbon dioxide–alcohol. Titration of the aqueous phase showed that it contained fluoride ion (0·4 mol.). Analytical gas chromatography of the organic phase (A) (dinonyl phthalate–kieselguhr 1 : 2, temp. 55°, nitrogen flow rate 1·0 l./hr.) gave peaks corresponding to perfluoro*cyclo*hexa-1 : 3-diene (after 9·5 min.), 1*H*-nonafluoro*cyclo*hex-1-ene (11·0 min.), and much unchanged decafluoride (15·0 min.). A small peak (after 22·0 min.) corresponded with that given by 3*H*-nonafluoro*cyclo*hex-1-ene.

Under identical conditions, undecafluoro*cyclo*hexane was completely dehydrofluorinated, fluoride ion (1·08 mol.) was found in the aqueous phase, and the organic product was shown by gas chromatography to be pure perfluoro*cyclo*hexene, no undecafluoro*cyclo*hexane being detected.

The organic phase (A) described above was re-treated with alkali under identical conditions. Fluoride ion (1·27 mol.) was found in the aqueous phase, and the starting material and 3*H*-nonafluoro*cyclo*hex-1-ene were no longer present in the product, which consisted of the 1 : 3-diene and the 1*H*-monoene.

It was shown by gas chromatography that 4*H*-nonafluoro*cyclo*hex-1-ene was not present in the dehydrofluorination product at any stage.

Preparative-scale work. The fluorohydrocarbon (10 g.), potassium hydroxide (10 g.), and water (10 c.c.) were shaken in a sealed tube at 100° for 3 hr. Analytical gas chromatography of the product (dinonyl phthalate–kieselguhr 1 : 2, temp. 55°, nitrogen flow rate 1·0 l./hr.) showed the presence of two components only, with peaks (after 9·5 and 11·0 min.) coincident with those given by perfluoro*cyclo*hexa-1 : 3-diene and 1*H*-nonafluoro*cyclo*hex-1-ene, respectively. Separation of the product (1 c.c. portions) was carried out in the preparative-scale column [4] (temp. 30°, nitrogen flow rate 9 l./hr.), the fractions appearing after 5 hr. and 5¼ hr. The first (16%) (Found : F, 68·7. Calc. for C_6F_8 : F, 67·8%) gave a single peak (after 9·5 min.) in analytical gas chromatography. It had two infrared bands, at 1710 and 1750 cm.$^{-1}$. The

patterns obtained from both techniques were identical with those given under the same conditions by an authentic specimen [3] of octafluoro*cyclo*hexa-1 : 3-diene.

The second fraction (80%) (Found : F, 69·8. Calc. for C_6HF_9 : F, 70·1%) gave a single peak (after 11·0 min.) from analytical gas chromatography. Infrared examination showed a single band at 1710 cm.$^{-1}$ (value quoted earlier [5] for 1*H*-nonafluoro*cyclo*hex-1-ene, 1707 cm.$^{-1}$).

Oxidation of 1H-*Nonafluoro*cyclo*hex*-1-*ene*.—The olefin (1·8 g.), potassium permanganate (12 g.), sodium hydrogen carbonate (6 g.), and water (30 c.c.) were heated at 120—130° for 15 hr. in a rocking autoclave. Isolation as usual gave crude dianilinium perfluoroadipate (3·0 g.), m. p. 209—211°. When recrystallised from acetone–chloroform it had m. p. 210—211° (recovery 86%) (Found : C, 45·1; H, 3·5; F, 31·6. Calc. for $C_{18}H_{16}O_4N_2F_8$: C, 45·4; H, 3·4; F, 31·9%). The m. p. obtained previously [3] was 210—212°.

Preparation of 1H : 2H-*Decafluoro*cyclo*hexanes from Perfluoro*cyclo*hexene*.—Chlorine was added to the olefin under ultraviolet irradiation.[5] 1 : 2-Dichlorodecafluoro*cyclo*hexane (25·0 g.) in ether (10 c.c.) was added to lithium aluminium hydride (5 g.) in ether (50 c.c.) which was stirred mechanically at 0°. After 1½ hr., water was added cautiously, followed by 50% sulphuric acid until no precipitate remained. The organic layer was separated, washed, dried, ($MgSO_4$), and distilled (1′ column) to remove ether. The residue was distilled from the flask (18·0 g.), and examination by analytical gas chromatography (dinonyl phthalate–kieselguhr 1 : 2) showed the presence of three components, a little ether, *trans*-1*H* : 2*H*-decafluoro*cyclo*hexane, and the *cis*-analogue. Separation in the preparative-scale gas chromatography column (5 portions, temp. 80°, nitrogen flow rate 9 l./hr.) afforded the *trans*-isomer (4·5 g.), b. p. 70°, m. p. 22—23° (Found : C, 27·3; H, 0·7; F, 71·5%), and the *cis*-isomer (11·4 g.), b. p. 91° (Found : F, 71·8%). In analytical gas chromatography, each of these fractions gave a single peak, coincident with those given by, respectively, the fraction from the fluorination product of benzene described earlier, and the sample, made from perfluoro*cyclo*hexene, reported previously.[5]

The *trans*-compound (0·36 g.), made as described above, and 9N-aqueous potassium hydroxide (0·72 c.c.) were shaken in a sealed tube at 100° for 1½ hr. Analytical gas chromatography of the product showed the presence of three components, perfluoro*cyclo*hexa-1 : 3-diene, 1*H*-nonafluoro*cyclo*hex-1-ene, and starting material. The same pattern was given by the sample isolated from the fluorination product of benzene when treated under identical conditions.

The *cis*-isomer, treated likewise, gave, on analytical chromatography, a single peak due to 1*H*-nonafluoro*cyclo*hex-1-ene with no starting material left. A very minor step at the start of the peak may have been due to perfluoro*cyclo*hexa-1 : 3-diene, but if present its concentration was below 1%.

Dipole Moments.—These were determined by the standard method from measurements of the dielectric constants of a number of dilute solutions of the compounds in benzene, with correction terms from the refractive indices of the solutions. Dielectric constants were measured by the "Resonance" method in an apparatus similar to that of Bender;[24] the refractive indices were measured by means of a Pulfrich critical-angle refractometer. The results were calculated by Guggenheim's method.[25] Measurements were made on perfluoro*cyclo*hexane as well as on the three fluorohydrocarbons, but in the former case only very dilute solutions in benzene could be made up (< 3% by wt.). Measurements on the undecafluoride were made with 4 solutions (concentrations, 4—12% by wt.); for the *cis*-decafluoride 4 solutions (2—6% by wt.); and for the *trans*-decafluoride 5 solutions (1·4—7% by wt.), were used. Measurements on chlorobenzene under similar conditions gave the expected value. Though no great accuracy can be claimed, the results enabled a clear distinction to be made between the *cis*- and the *trans*-form.

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[24] Bender, *J. Chem. Educ.*, 1946, **23**, 179.
[25] Guggenheim, *Trans. Faraday Soc.*, 1949, **45**, 714; 1951, **47**, 573.

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488. *The Oxidation of Phenylhydrazine.*

By R. L. Hardie and R. H. Thomson.

A new method of phenylation is described, namely, oxidation of phenylhydrazine with metallic oxides (preferably silver) in an aromatic solvent. Phenyl radicals are the active species. Similar reactions have been effected with four other arylhydrazines. Diaryls are also formed by the oxidation of phenylhydrazine with air, and with benzoquinones, in aromatic solvents, and with silver oxide and cupric sulphate in aqueous media.

It is well known that phenylhydrazine is extremely sensitive to oxidation and this phenomenon was the subject of numerous early investigations. Many different oxidising agents [1] have been used and a variety of products is formed according to the reagent and the conditions. Nearly all previous oxidations have been conducted in aqueous media, although Fischer and Ehrhard [2] oxidised phenylhydrazine with mercuric oxide in ether, obtaining aniline, diphenyl, mercury, and nitrogen, and Chattaway examined the effect of oxygen [3] and certain metallic oxides,[4] in the absence of a solvent, obtaining nitrogen, benzene, a little diphenyl, and traces of other substances. This paper is mainly concerned with the oxidation of phenylhydrazine in aromatic solvents, which has not been studied hitherto.

The oxidations were effected by gradual addition of the equivalent amount of silver oxide to a solution of phenylhydrazine in an aromatic solvent. Yellow mercuric oxide is a more vigorous oxidant but the reaction is complicated by the formation of arylmercury compounds; in both cases it is necessary to control the reaction by cooling, indeed on one occasion an uncontrolled oxidation mixture with mercuric oxide in benzene caught fire. Cupric oxide and lead dioxide are much less effective and heating is necessary to start the reaction. The principal oxidation products are nitrogen, water, and a mixture of diaryls. The latter are of most interest and the minor products were not isolated in every experiment but we found that benzene was formed when the oxidation was done in bromobenzene and in nitrobenzene, and this is doubtless a normal product. A similar oxidation of 2-naphthylhydrazine in benzene gave naphthalene as well as 2-phenylnaphthalene. Usually a trace of azobenzene was isolated by chromatography and in reactions on a larger scale (15 g. of phenylhydrazine) diphenyl was detected. Mercuric oxide gave diphenylmercury in addition and, if used in excess, some phenylmercuric chloride. This probably arose from a trace of mercuric chloride in the sample of oxide and when mercuric chloride was deliberately added phenylmercuric chloride was the major product. The oxidations are not quantitative. A series of nitrogen determinations carried out on the oxidation of phenylhydrazine with silver oxide in bromobenzene showed that only 65—70% of the theoretical volume was liberated, and acid extraction of the reaction mixture yielded unchanged phenylhydrazine (*ca.* 10%). Attempts to improve the efficiency of the oxidation by raising the temperature at the end of reaction are hampered by the thermal instability of phenylhydrazine. Aniline is formed and the amount of azobenzene increases. It seems likely that the azobenzene usually obtained arises from a little aniline in the phenylhydrazine but we were unable to obtain a sample of the latter which gave no trace of azobenzene. Probably slight decomposition occurs during distillation, even at very low pressure. A little *p*-nitroaniline was isolated on oxidation of *p*-nitrophenylhydrazine in warm benzene; in this case heating is necessary as the hydrazine is rather insoluble in benzene and the reaction is very slow in cold suspension.

The diaryls obtained in different solvents are listed in Table 1; a mixture of isomers was obtained in all cases (except in benzene) but on the usual scale of operation (5 g. of

[1] Seide, Scherlin, and Bras, *J. prakt. Chem.*, 1933, **138**, 55, and references therein.
[2] Fischer and Ehrhard, *Annalen*, 1879, **199**, 332.
[3] Chattaway, *J.*, 1907, **91**, 1323.
[4] Chattaway, *J.*, 1908, **93**, 270.

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phenylhydrazine) it was only possible to isolate a few individual compounds as indicated. The formation of these compounds suggests that the oxidation of phenylhydrazine under

TABLE 1. *Oxidation of phenylhydrazine with silver and mercuric oxides.*

Solvent	Phenylation products isolated
Benzene	Diphenyl
Toluene	Mixed methyldiphenyls
*iso*Propylbenzene *	Mixed *iso*propyldiphenyls
Nitrobenzene	2- and 4-Nitrodiphenyl
Chlorobenzene	2-Chlorodiphenyl
Bromobenzene	4-Bromodiphenyl
Anisole †	Mixed methoxydiphenyls
Pyridine	2-, 3-, and 4-Phenylpyridines ‡

* Silver oxide only in this solvent. ‡ Isolated as their picrates.
† Mercuric oxide only in this solvent.

these conditions produces phenyl radicals which then attack the solvent, and this is strongly supported by the following evidence. (1) The products formed by oxidation of phenylhydrazine with silver oxide in *iso*propylbenzene include 2 : 3-dimethyl-2 : 3-diphenylbutane. This arises by the abstraction of an α-hydrogen atom from *iso*propylbenzene and dimerisation of the resulting radical, and its formation establishes the homolytic nature of this reaction.[5] (2 : 3-Dimethyl-2 : 3-diphenylbutane is not formed by the action of silver oxide alone on *iso*propylbenzene.) (2) Infrared analysis [6] of the mixture of chlorodiphenyls obtained by oxidising phenylhydrazine with silver oxide in chlorobenzene shows that the ratio of isomers formed is in agreement, having regard to the accuracy of the analytical method, with those obtained by Augood, Hey, and Williams [6] for the phenylation of chlorobenzene by benzoyl peroxide, and by means of the Gomberg reaction, and by Bryce-Smith and Clarke [7] using silver iodide dibenzoate (see Table 2). We conclude that the active species, namely, the phenyl radical, is the same in each case

TABLE 2. *Phenylation of chlorobenzene. Isomer ratios* (%).

Method	*ortho*	*meta*	*para*
Benzoyl peroxide [6]	60·3	25·9	13·75
Gomberg [6]	64·55	21·7	13·7
Silver iodide dibenzoate [7]	60·0	24·0	16·0
Phenylhydrazine–silver oxide	64·9	22·1	13·0

and the silver oxide oxidation of phenylhydrazine therefore joins the growing list [8] of methods available for the phenylation of aromatic compounds. The reaction can be most simply represented as follows :

$$Ph{\cdot}NH{\cdot}NH_2 \xrightarrow{Ag_2O} [Ph{\cdot}N{:}NH] \longrightarrow N_2 + Ph\cdot + H\cdot \longrightarrow PhH$$

$$+ H_2O + 2Ag \qquad Ph\cdot + Ph_2 \qquad Ph\cdot + ArH \rightarrow Ph{\cdot}Ar$$

The formation of diphenyl is shown as arising by dimerisation of phenyl radicals. This minor product was first detected in oxidation products obtained in bromobenzene and in this instance it could conceivably be formed by phenyl radicals attacking the bromobenzene with displacement of bromine. To test this, phenylhydrazine was oxidised with silver oxide in [^{14}C]bromobenzene. The diphenyl obtained was very feebly active, which seems to imply that a very small proportion of the phenyl radicals do behave in this way.

[5] Kharasch, McBay, and Urry, *J. Org. Chem.*, 1945, **10**, 401.
[6] Augood, Hey, and Williams, *J.*, 1953, 45.
[7] Bryce-Smith and Clarke, *J.*, 1956, 2264.
[8] References to five methods are given by Hey, Nechvatal, and Robinson, *J.*, 1951, 2892. For others see Hey, Stirling, and Williams, *J.*, 1954, 2747; 1956, 1475; Sandin and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 2253; and ref. 7.

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In addition to the reaction scheme postulated above it is possible that oxidation of the phenylhydrazine may lead to the diazo-compound, Ph·N:N·OH, homolysis of which would yield hydroxyl as well as phenyl radicals. As yet we have obtained no definite evidence in favour of this. The formation of hydroxyl radicals in the presence of aromatic solvents has usually been detected by isolation of the appropriate phenols but this method is not very suitable under the present conditions as the phenols, if formed, would also be susceptible to oxidation. We have shown that *p*-cresol is oxidised to a tetrahydro-oxodibenzofuran derivative with silver oxide in benzene, and such products would of course react further with phenylhydrazine. In practice alkaline extraction of oxidation mixtures usually gave a few mg. of solid having a definite phenolic odour but we have not been able to identify any of these products. Phenol was obtained on oxidation of phenylhydrazine in benzene when the mixture was boiled after the reaction but this in inconclusive. In these circumstances phenol could arise by interaction of phenyl radicals and hot water.

Yields of phenylated products are usually low and as a preparative method there is no advantage over older procedures, but where a substituted phenylhydrazine is available it may occasionally be useful. Some examples are shown in Table 3.

TABLE 3. *Oxidation of arylhydrazines with silver oxide in benzene.*

Hydrazine	Product	Yield (%)
p-Bromophenyl	4-Bromodiphenyl	36
p-Nitrophenyl	4-Nitrodiphenyl	28
2 : 4-Dinitrophenyl	2 : 4-Dinitrodiphenyl	39
2-Naphthyl	2-Phenylnaphthalene	9·5
p-Nitrophenyl (in thiophen solution)	2-*p*-Nitrophenylthiophen	13

It has long been known that phenylhydrazine does not react normally with benzoquinones, *i.e.*, phenylhydrazones are not formed. Instead the quinone is reduced to a quinol with the liberation of nitrogen and the reaction, using phenylhydrazine " carbamate," was adapted by Willstätter and Cramer [9] for use as a gasometric method for the estimation of quinones. This reaction, in aromatic solvents, appears to take the same course as the silver oxide oxidation, producing phenyl radicals which then attack the solvent. When benzene solutions of phenylhydrazine and benzoquinone (or chloranil) were mixed at room temperature there was a vigorous evolution of nitrogen and the quinol separated. Diphenyl and a trace of azobenzene were isolated from the benzene solution. Similarly 4-nitrodiphenyl was obtained on oxidation of phenylhydrazine with chloranil in nitrobenzene at room temperature, and in *iso*propylbenzene 2 : 3-dimethyl-2 : 3-diphenylbutane and diphenyl were detected in addition to the *iso*propyldiphenyls.

Aerial oxidation of phenylhydrazine is of a similar character to those described above. This reaction was studied by Chattaway [3] who exposed filter paper saturated with phenylhydrazine to oxygen. Nitrogen was evolved readily but the only other product isolated was benzene. On bubbling oxygen through a solution of phenylhydrazine in *iso*propylbenzene much tar is produced from which we have been able to isolate a little 2 : 3-dimethyl-2 : 3-diphenylbutane besides azobenzene and mixed *iso*propyldiphenyls. A similar oxidation in pyridine afforded 4-phenylpyridine.

From the nature of the products isolated most of the oxidations of phenylhydrazine which have been effected in aqueous solution seem to be ionic. Intermediate diazo-compounds are probably formed which then decompose in the expected fashion. In some cases there is definite evidence for the formation of diazonium salts, *e.g.*, in oxidations with chlorine or bromine,[10] or with iodate in acid solution.[11] Most of these reactions are of theoretical interest only, but the use of cupric sulphate in boiling aqueous solution is of practical value [12] for the removal of hydrazino-groups, $Ar{\cdot}NH{\cdot}NH_2 \longrightarrow ArH$. A brief

[9] Willstätter and Cramer, *Ber.*, 1910, **43**, 2976.
[10] Chattaway, *J.*, 1908, **93**, 852.
[11] Miller and Furman, *J. Amer. Chem. Soc.*, 1937, **59**, 161.
[12] Cf. Schofield and Swain, *J.*, 1950, 392.

examination has shown that this oxidation, and possibly others in neutral aqueous solution, are, at least in part, homolytic reactions: for diphenyl (and benzene) was formed when phenylhydrazine was oxidised with cupric sulphate in hot water, and phenylpyridines (the 2- and the 4-isomer were isolated as their picrates) when the same oxidation was conducted in aqueous pyridine. Similar oxidations of phenylhydrazine with silver oxide in water, and in aqueous pyridine, yielded small amounts of diphenyl and 4-phenylpyridine, respectively.

Experimental

Solvents were purified as described by Hey *et al.*[6, 13] and Bryce-Smith and Clarke.[7] Chromatographic separations were done on alumina with light petroleum (b. p. 50—60°) as solvent. Products were identified by mixed m. p. determinations unless otherwise indicated.

Oxidation of Phenylhydrazine with Silver Oxide.—General procedure. To a vigorously stirred solution of phenylhydrazine (5 g.) in an aromatic solvent (150 ml.), cooled in ice-water, silver oxide (11 g.) was added gradually. Stirring was continued for 30 min., by which time the reaction had subsided, and the mixture was then left overnight at room temperature. The silver residue was filtered off and washed with the solvent, and the combined filtrates were dried ($MgSO_4$). Unless otherwise stated, the solvent was removed by distillation *in vacuo* through a helix-packed column, and the residual oil worked up as detailed below.

(i) *In benzene.* (*a*) Hydrochloric acid extraction of the reaction mixture (from 10 g. of phenylhydrazine) yielded unchanged phenylhydrazine (1·2 g.). Chromatography of the residue after removal of the solvent gave diphenyl (0·8 g.), m. p. 69°, and azobenzene (0·3 g.), m. p. 68°. (*b*) The above experiment was repeated and the oxidation mixture finally boiled under reflux for 30 min. Extraction of the benzene solution with 2N-aqueous sodium hydroxide then gave phenol (0·14 g.) (benzoate, m. p. 69°). Further extraction with dilute hydrochloric acid yielded a mixture of phenylhydrazine (0·4 g.) and aniline (0·2 g.) (benzanilide, m. p. 161°), separated by fractional distillation.

(ii) *In chlorobenzene.* (*a*) Distillation gave a light red oil (2·5 g.), b. p. 120—150°/7 mm., which was chromatographed, yielding azobenzene (0·13 g.) and a yellow oil (1·1 g.), crystallisation of which from alcohol gave 2-chlorodiphenyl (0·36 g.), m. p. 34°. (*b*) The oxidation was repeated on a larger scale (4 × 15 g. of phenylhydrazine) to obtain a mixture of isomeric chlorodiphenyls for infrared analysis. Azobenzene was removed from the initial light red oil by catalytic reduction and extraction of aniline with dilute hydrochloric acid. Distillation then gave diphenyl and a light yellow oil, b. p. 82—100°/0·2 mm., which was further purified by chromatography.

(iii) *In bromobenzene.* (*a*) 15 G. of phenylhydrazine were used. Before being worked up the reaction mixture was extracted with hydrochloric acid which gave unchanged phenylhydrazine (1·2 g.) but no aniline. Carbon tetrachloride (60 ml.) was then added to the solution and a fraction, b. p. 70—80°, was collected by distillation. This was nitrated by dropwise addition of a mixture of fuming nitric acid (10 ml.) and concentrated sulphuric acid (10 ml.). After being heated under reflux for 15 min. the solution was poured on ice. Crystallisation of the precipitate from aqueous alcohol gave *m*-dinitrobenzene, m. p. 90° (1·6 g., equiv. to 0·74 g. of benzene). The mixture was then filtered and worked up in the usual way. Chromatography of the initial oil (2·9 g.; b. p. 100—125°/1·5 mm.) gave a light yellow oil (1·8 g.) which on distillation yielded diphenyl (0·55 g.) and mixed bromodiphenyls (0·95 g.), b. p. 90—100°/0·03 mm., which crystallised from alcohol, yielding 4-bromodiphenyl (0·3 g.), m. p. 89°. (*b*) The reaction was repeated with phenylhydrazine (15 g.) in [^{14}C]bromobenzene (200 ml.; activity 1·5 μc/mole). The solutions from four such oxidations were combined and the diphenyl was isolated as in (*a*). It was freed from radioactive solvent by repeated chromatography, distillation, and final crystallisation from light petroleum (b. p. 30—40°). The activity was $2·7 \times 10^{-7}$ μc/mole.

(iv) *In nitrobenzene.* (*a*) Extraction of the reaction mixture (from 10 g. of phenylhydrazine) with dilute hydrochloric acid yielded unchanged phenylhydrazine (1 g.). Benzene was isolated by distillation with carbon tetrachloride and converted into *m*-dinitrobenzene (1 g., equiv. to 0·46 g. of benzene). The crude product obtained on removal of the solvent distilled to a light red oil (4·2 g.), b. p. 90—150°/0·2 mm. Chromatography gave diphenyl (0·3 g.), azobenzene (0·3 g.), mixed nitrodiphenyls as a yellow oil (1·7 g.), and the 4-isomer (0·9 g.). (*b*) The combined products from several oxidations (60 g. of phenylhydrazine in all) were distilled, giving a red oil

[13] Hey, Pengilly, and Williams, *J.*, 1956, 1463; Hey, Stirling, and Williams, *J.*, 1955, 3963.

(11·8 g.), b. p. 100—140°/8 mm., and a fraction (5 g.), b. p. 150—160°/8 mm., which solidified. The latter, 4-nitrodiphenyl, crystallised from alcohol in light yellow needles, m. p. 113°. A chromatogram of the red oil yielded (1) diphenyl (1·2 g.), (2) azobenzene (0·9 g.), (3) 2-nitrodiphenyl (1·2 g.), m. p. 36° (from alcohol), (4) a yellow oil (1·5 g.) (mixed nitrodiphenyls), and (5) 4-nitrodiphenyl (2·7 g.).

(v) *In* iso*propylbenzene*. The crude product from phenylhydrazine (15 g.) in *iso*propylbenzene (150 ml.) distilled as a light yellow oil (4·8 g.), b. p. 85—150°/2·5 mm. Chromatography then yielded (1) diphenyl (0·3 g.), (2) 2 : 3-dimethyl-2 : 3-diphenylbutane (0·5 g.), m. p. 118° (Found : C, 90·7; H, 9·1. Calc. for $C_{18}H_{22}$: C, 90·75; H, 9·25%), and (3) mixed *iso*propyldiphenyls as a light yellow oil, b. p. 80—100°/0·15 mm. (0·9 g.) (Found : C, 91·5; H, 8·0. Calc. for $C_{15}H_{16}$: C, 91·8; H, 8·2%).

(vi) *In pyridine*. Distillation gave a mixture of phenylpyridines (0·95 g.), b. p. 110—130°/0·2 mm., and azobenzene (0·1 g.). Conversion of the phenylpyridines into their picrates and fractional crystallisation from acetone gave the 2-isomer (0·14 g.), m. p. 175°, the 3-isomer (0·08 g.), m. p. 160°, and the 4-isomer (0·13 g.), m. p. 195°.

(vii) *In toluene*. The crude product from the oxidation of phenylhydrazine (10 g.) in toluene (200 ml.) distilled as a light yellow oil (2 g.), b. p. 90—120°/3 mm. A chromatogram yielded diphenyl (50 mg.) and a mixture of methyldiphenyls (1·5 g.), b. p. 77—84°/0·3 mm. (Found : C, 92·5; H, 7·2. Calc. for $C_{13}H_{12}$: C, 92·85; H, 7·15%).

Oxidation of Phenylhydrazine with Mercuric Oxide.—General procedure. Mercuric oxide (10 g.) was added gradually to a vigorously stirred solution of phenylhydrazine (5 g.) in an aromatic solvent (150 ml.), cooled in ice-water. A brisk evolution of nitrogen took place and mercury and water separated. The mixture was left overnight at room temperature, the mercury residue was filtered off and washed with solvent, and the combined filtrates were dried ($MgSO_4$). The solvent was then removed by distillation *in vacuo* through a helix-packed column, and the product worked up as indicated below.

(1) *In benzene*. (*a*) The residue crystallised from alcohol, yielding diphenylmercury (1·35 g.) as plates, m. p. 125°. Steam-distillation of the concentrated alcohol mother-liquor gave diphenyl (0·7 g.). (*b*) The reaction was repeated with the addition of mercuric chloride (1 g.). After being kept overnight, the mixture was boiled under reflux for 10 min. and filtered hot. On cooling, phenylmercuric chloride (3 g.), m. p. 254°, separated. The solvent was removed by distillation and extraction of the residue with ether left more ether-insoluble phenylmercuric chloride (1·5 g.). Working up the ethereal solution as above gave diphenylmercury (1·5 g.) and diphenyl (0·5 g.).

(ii) *In chlorobenzene*. Extraction of the residue with light petroleum (b. p. 50—60°) left the insoluble diphenylmercury (1·45 g.). The red oil obtained on removal of the light petroleum was distilled, yielding a light red oil (0·6 g.), b. p. 120—150°/7 mm. When crystallised from ethanol it gave 2-chlorodiphenyl (0·13 g.) as light yellow prisms, m. p. 34°.

(iii) *In bromobenzene*. Diphenylmercury (0·9 g.) was isolated as in (i). Removal of the light petroleum and distillation of the residue gave a light red oil (2·0 g.), b. p. 100—140°/7 mm. Chromatography of this afforded azobenzene (0·1 g.) and a yellow oil (0·8 g.) (mixed bromodiphenyls) (Found : C, 62·6; H, 4·25. Calc. for $C_{12}H_9Br$: C, 61·8; H, 3·9%).

(iv) *In nitrobenzene*. The residue on distillation gave a light red oil (2·9 g.), b. p. 100—160°/0·05 mm. Chromatography yielded phenylmercuric chloride (0·1 g.), azobenzene (0·22 g.), and a mixture of nitrodiphenyls (1·1 g.) which, on fractional crystallisation from alcohol, yielded the 2- and the 4-isomer.

(v) *In pyridine*. Diphenylmercury (1·28 g.) was isolated as above. Distillation of the residue gave a mixture of phenylpyridines (0·95 g.), b. p. 115—120°/0·15 mm. All three isomers were isolated, as their picrates, by fractional crystallisation.

(vi) *In anisole*. The initial products were diphenylmercury (1·5 g.) and a light red oil (0·98 g.), b. p. 130—140°/7 mm. Chromatography of this gave azobenzene (0·15 g.) and mixed methoxydiphenyls as a faintly yellow oil (0·5 g.) (Found : C, 84·7; H, 6·4. $C_{13}H_{12}O$ requires C, 84·8; H, 6·4%).

Oxidation of Phenylhydrazine with Other Metallic Oxides.—Cupric oxide. The oxide (11 g.) was added to a solution of phenylhydrazine (5 g.) in pyridine (200 ml.) and the suspension warmed to 50—60° until reaction began. Working up as before gave a mixture of phenylpyridines (0·8 g.), b. p. 120—130°/0·2 mm. All three isomers were separated by fractional crystallisation of their picrates.

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Lead dioxide. Repetition of the above experiment, but with lead dioxide (8 g.), gave a mixture of the three phenylpyridines (1·5 g.) which were separated as their picrates.

Oxidation of Other Arylhydrazines with Silver Oxide.—(i) To a vigorously stirred solution of *p*-bromophenylhydrazine (1·8 g.) in benzene (100 ml.), silver oxide (4 g.) was added gradually. Then the mixture was boiled under reflux for 30 min. and left overnight. Working up in the usual way and distillation of the crude product gave a colourless oil, b. p. 100—120°/2 mm., which solidified. Crystallisation from alcohol gave 4-bromodiphenyl as colourless needles, m. p. 88° (0·7 g.) (Found: C, 62·1; H, 4·0; Br, 33·5. Calc. for $C_{12}H_9Br$: C, 61·8; H, 3·85; Br, 34·3%).

(ii) (*a*) Oxidation of a warm suspension of *p*-nitrophenylhydrazine (5 g.) in benzene (200 ml.) as in (i) gave, after removal of the solvent, a solid residue. Crystallisation from alcohol gave 4-nitrodiphenyl as light yellow needles, m. p. 113° (1·8 g.). (*b*) In another experiment using 10 g. of *p*-nitrophenylhydrazine, extraction of the benzene solution with dilute hydrochloric acid gave *p*-nitroaniline (0·3 g.) (acetyl derivative, m. p. 216°).

(iii) Oxidation of a warm suspension of 2 : 4-dinitrophenylhydrazine (5 g.) in benzene (200 ml.) and working up as above gave a solid product. Extraction with ether left a little unchanged 2 : 4-dinitrophenylhydrazine. Removal of the ether yielded 2 : 4-dinitrodiphenyl which crystallised from alcohol as orange plates, m. p. 110° (2 g.) (Found: C, 59·0; H, 3·6; N, 11·6. Calc. for $C_{12}H_8O_4N_2$: C, 59·0; H, 3·3; N, 11·5%).

(iv) Oxidation of *p*-nitrophenylhydrazine (10 g.) in thiophen (200 ml.) and chromatography of the product using ether–light petroleum (1 : 1) gave 2-*p*-nitrophenylthiophen, m. p. 138° (1·7 g.) (Found: C, 58·2; H, 3·4; N, 6·5. Calc. for $C_{10}H_7O_2NS$: C, 58·3; H, 3·4; N, 6·8%). From two other bands were obtained (1) orange *leaflets*, m. p. 210° (0·3 g.), possibly 2 : 5-di-*p*-nitrophenylthiophen (Found: C, 57·8; H, 3·2. $C_{16}H_{10}O_4N_2S$ requires C, 58·8; H, 3·05%), and (2) a bright red solid, m. p. 258° (0·1 g.) (from alcohol).

(v) (*a*) Oxidation of 2-naphthylhydrazine (6 g.) in benzene (200 ml.) in the usual way gave a crude product which yielded on distillation naphthalene (1·4 g.), b. p. 60—70°/2·5 mm., m. p. 79° (from alcohol), and 2-phenylnaphthalene (0·7 g.), b. p. 120—125°/2·5 mm., m. p. 101° (from alcohol). (*b*) A similar oxidation using an excess of mercuric oxide and 2-naphthylhydrazine (3·5 g.) gave naphthalene (0·8 g.), 2-phenylnaphthalene (0·4 g.), and 2-naphthylmercuric chloride (0·6 g.), m. p. 268°.

Oxidation of Phenylhydrazine with Quinones.—General procedure. To a vigorously stirred solution of phenylhydrazine (5 g.) in an aromatic solvent (200 ml.) was added an equivalent quantity of the quinone. Vigorous evolution of nitrogen took place and immediate separation of the quinol. The mixture was boiled under reflux for 1 hr., cooled, and filtered. The solvent was then removed by distillation *in vacuo* and the residue worked up in the usual way.

(i) *Benzoquinone in benzene.* Quinol (4·5 g.) was collected and the benzene solution yielded diphenyl (0·4 g.) and a trace of azobenzene.

(ii) *Chloranil in benzene.* The products were tetrachloroquinol (11 g.), diphenyl (0·6 g.), and a trace of azobenzene.

(iii) *Chloranil in nitrobenzene.* 10 G. of phenylhydrazine were used (the mixture was *not* heated after the addition of the quinone). Tetrachloroquinol separated and distillation of the residue obtained on removal of the solvent gave 4-nitrodiphenyl (0·2 g.), m. p. 113°.

(iv) *Chloranil in* iso*propylbenzene.* The volatile product from 15 g. of phenylhydrazine distilled at 80—130°/2 mm. (1·1 g.) and was separated by chromatography into diphenyl (0·05 g.), 2 : 3-dimethyl-2 : 3-diphenylbutane (0·1 g.), and a light yellow oil (0·6 g.) (mixed *iso*propyldiphenyls).

Oxidation of Phenylhydrazine in Aqueous Media.—(i) *Silver oxide in water.* The oxide (30 g.) was added gradually to a vigorously stirred suspension of phenylhydrazine (15 g.) in water (200 ml.) cooled in ice-water. The mixture was then kept at 60—70° for 30 min. Benzene was isolated by distillation with carbon tetrachloride and was converted into *m*-dinitrobenzene (5·0 g., equiv. to 2·3 g. of benzene). Subsequent steam-distillation of the reaction mixture yielded diphenyl (60 mg.).

(ii) *Silver oxide in aqueous pyridine.* Silver oxide (20 g.) was added to a vigorously stirred solution of phenylhydrazine (10 g.) in pyridine (100 ml.) and water (100 ml.). Next day the mixture was refluxed for 30 min. and filtered. Removal of the solvents left a residue which distilled as a yellow oil (2·3 g.), b. p. 90—120°/0·1 mm., and from this 4-phenylpyridine was isolated as its picrate (0·3 g.).

(iii) *Cupric sulphate in water.* A solution of cupric sulphate (40 g.) in water (300 ml.) was added gradually with stirring to a solution of phenylhydrazine (15 g.) in boiling water (200 ml.). Boiling under reflux was continued for 30 min. after the addition was complete. Benzene was isolated as the dinitro-derivative (equiv. to 1·2 g. of benzene) as in (i), and diphenyl (0·17 g.) was obtained by steam-distillation.

(iv) *Cupric sulphate in aqueous pyridine.* As in (iii) cupric sulphate solution was added to phenylhydrazine (10 g.) in aqueous pyridine at 60—70°. Distillation as before yielded benzene (1·9 g.; isolated as the dinitro-derivative). Removal of the solvent and distillation of the residue gave a yellow oil (0·7 g.), b. p. 90—120°/0·1 mm., from which 2- and 4-phenylpyridine were isolated as their picrates.

Oxidation of Phenylhydrazine with Oxygen.—(i) *In* iso*propylbenzene.* A slow stream of oxygen was passed through a solution of phenylhydrazine (20 g.) in *iso*propylbenzene (300 ml.) for 40 hr. Removal of the solvent left a tar which distilled to a red oil (2·7 g.), b. p. 70—110°/0·7 mm. Chromatography gave azobenzene (0·5 g.) and a light yellow oil (0·7 g.) from which 2 : 3-dimethyl-2 : 3-diphenylbutane (20 mg.) was precipitated on addition of nitromethane. Removal of the nitromethane and distillation of the residue gave a light yellow oil (0·4 g.), b. p. 80—100°/0·15 mm. (Found: C, 91·7; H, 8·0. Calc. for $C_{15}H_{16}$: C, 91·8; H, 8·2%).

(ii) *In pyridine.* The reaction was carried out as in (i). The product was a yellow oil (0·9 g.), b. p. 80—115°/0·05 mm., from which 4-phenylpyridine was isolated as its picrate.

Oxidation of p-*Cresol.*—Silver oxide (10 g.) was added to a solution of *p*-cresol (5 g.) in benzene (100 ml.), and the mixture left overnight, then boiled under reflux for 15 min., cooled, and filtered. The product, after removal of the solvent, was steam-distilled to remove unchanged cresol (3·1 g.). Extraction of the residue with ether and then distillation gave a gum (0·5 g.), b. p. 210—230°/0·5 mm. Treatment of the latter with 5% sodium hydroxide solution precipitated the ketone [14] which formed a phenylhydrazone, m. p. 181° (0·15 g.).

We are indebted to Professor D. H. Hey, F.R.S., and Dr. G. H. Williams for samples of the nitro- and chloro-diphenyls and the phenylpyridine picrates, and to Dr. Neil Campbell for a specimen of 2-phenylnaphthalene. We also thank Dr. J. C. Bevington for the radioactive assay, Dr. D. C. McKean for helpful advice on the infrared analyses, and Dr. R. A. Chalmers and Miss D. A. Thomson for the microanalyses. One of us (R. L. H.) thanks the University of Aberdeen for a Scholarship.

THE UNIVERSITY, OLD ABERDEEN, SCOTLAND. [*Received, January 1st,* 1957.]

[14] Pummerer, Melamed, and Puttfarcken, *Ber.*, 1922, **55**, 3116; Pummerer, Puttfarcken, and Schopflocher, *Ber.*, 1925, **58**, 1808.

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489. *Electrophilic Substitution. Part X.* Nitration of Quinoxaline.*

By M. J. S. DEWAR and P. M. MAITLIS.

Quinoxaline has been shown to be mononitrated in the 5-position and dinitrated in the 5 : 6-positions.

APART from the formation of yellow crystals from quinoxaline by concentrated nitric acid which Hinsberg [1] suggested might be those of a nitro-derivative, no work has been reported on the nitration of quinoxaline. This base has always been assumed to be feebly reactive with electrophilic reagents, in view of the strong deactivating effect of the two nitrogen atoms. After several failures under milder conditions we found a mixture of oleum and nitric acid at 90° to give a mononitro- (1·5%) and a dinitro-quinoxaline (I) (24%). The former, m. p. 94—95°, must be 5-nitroquinoxaline, for which Schultz [2] gives m. p. 95—96°, since the only other isomer (6-) which could reasonably be formed

* Part IX, *J.*, 1957, 944.

[1] Hinsberg, *Ber.*, 1884, **17**, 320.
[2] Schultz, *J. Amer. Chem. Soc.*, 1950, **72**, 3824.

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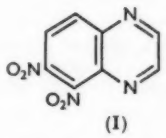
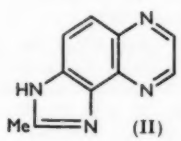
has m. p. 177°.[3] The compound (I) must therefore be a 5 : *x*-dinitroquinoxaline. This structure was confirmed by reduction with hydrazine hydrate and palladised charcoal, followed by acetylation: the only product isolated was 5-acetamidoquinoxaline.[4] Since the acetylation of the diaminoquinoxaline was shown to proceed smoothly, the extra nitro-group must have been lost during the reduction.


(I)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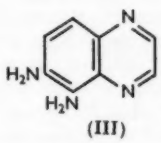
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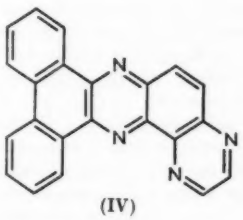
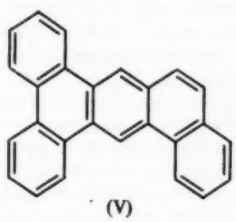
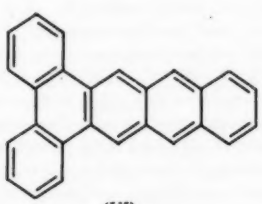

(IV)


(V)


(VI)

Reduction with iron powder and glacial acetic acid, followed immediately by acetylation, gave a methylquinoxalinoglyoxaline (II), suggesting that the two original nitro-groups (assuming no molecular rearrangement had occurred) were *ortho* to each other. The reduction was then repeated and the products were separated at the amine stage by chromatography into a small amount of the tricyclic compound (II) and the crude diamine (III). The last, with phenanthraquinone, formed a condensation product which with sulphuric acid gave the red colour typical of dibenzophenazine derivatives; its analysis was that of the expected compound (IV). The spectrum of this compound (IV) in carbon tetrachloride does not agree exactly with that of 1 : 2-3 : 4-5 : 6-tribenzanthracene [5a] (V), in contrast to the frequent correspondence observed between heterocycles and isoconjugate hydrocarbons; [6] nevertheless the bands in compound (IV) at 401, 390, 379·5, 359·5, and 322 mμ correspond quite closely to the bands in the hydrocarbon (V) at 387·5, 377, 368, 345, and 303 mμ. Allowing for the difference in intensity of the various peaks, a bathochromic shift of *ca.* 13 mμ for the hydrocarbon would make the spectra superimposable. This is a much closer correspondence than that between the compounds (IV) and (VI).[5b]

Reductive acetylation of the dinitro-compound (I) in the presence of excess of acetic anhydride gave a diacetamidoquinoxaline. It was not possible to convert this into the glyoxaline (II) by treatment with hydrochloric acid, the starting material being recovered unchanged. Aqueous alkali destroyed the molecule.

A product isolated on nitration of quinoxaline with nitric acid and trifluoracetic anhydride gave analyses for a hydroxynitroquinoxaline, but did not correspond to any of the known isomers.

Experimental

Microanalyses were by the Microanalytical Laboratory, Imperial College of Science and Technology, London. The spectrum of the compound (IV) was measured in "AnalaR" carbon tetrachloride on a Unicam S.P. 500 spectrophotometer.

[3] Beilstein's "Handbuch der organischen Chemie," Vol. XXIII, p. 177.
[4] Landquist, *J.*, 1953, 2816.
[5] Clar, "Aromatische Kohlenwasserstoffe," Springer Verlag, Berlin, 1952, 2nd Edn., pp. (*a*) 205, (*b*) 242.
[6] Badger *et al.*, *J.*, 1951, 3199; 1956, 122.

Nitration of Quinoxaline.—To a solution of quinoxaline [7] (11 g.) in sulphuric acid (50 ml.) was added (*a*) a mixture of nitric acid (*d* 1·5; 25 ml.) and sulphuric acid (50 ml.) and (*b*) oleum (65% of SO_3; 50 ml.). Solutions were made with strong cooling, usually in acetone–solid carbon dioxide. The final mixture was heated on a steam-bath at 85—90° for 24 hr., then allowed to cool to room temperature and hydrolysed by being poured on ice (2 kg.) whereupon a sticky orange solid separated. (Addition of alkali caused this solid to dissolve, the solution becoming deep red; the original solid could not then be recovered on acidification.) The solid was extracted with chloroform containing acetone (20% v/v; 10 × 200 ml.); evaporation of the dried extract left a tar (12 g.), which was taken up in the minimum amount of acetone (30 ml.), boiled with charcoal, filtered, and allowed to crystallise. Recrystallisation gave yellow prisms (5·1 g.), m. p. 172—173°, of 5 : 6-*dinitroquinoxaline* (Found: C, 43·0; H, 2·0; N, 25·6; *M*, 225. $C_8H_4O_4N_4$ requires C, 43·6; H, 1·8; N, 25·5%; *M*, 220). The mother-liquors were evaporated to dryness and the residue was chromatographed on alumina in benzene to give a yellow solution. Evaporation and recrystallisation gave the same compound (I) (0·2 g.) and 5-*nitroquinoxaline* (0·3 g.), m. p. 80—85°. This crystallised from aqueous alcohol in pale yellow needles, which after vacuum-sublimation had m. p. 95—96° (Found: C, 54·4; H, 3·2; N, 23·8%. Calc. for $C_8H_5N_3O_2$: C, 54·8; H, 2·8; N, 24·0%). Only a small amount of quinoxaline (0·4 g.) was recovered by neutralising the original solution.

Orientation of the 5 : x-*Dinitroquinoxaline.*—(a) *Reduction with hydrazine hydrate.* Hydrazine hydrate (3 ml.) and 10% palladised charcoal (50 mg., in portions, during 10 min.) were added to a solution of the nitro-compound (I) (0·9 g.) in ethanol (40 ml.) at 70°. After 30 min. the solution was filtered and evaporated. The product was warmed for 5 min. with acetic anhydride (10 ml.) and concentrated sulphuric acid (0·1 ml.) on a steam-bath. The mixture was neutralised and extracted with chloroform, and the extract chromatographed on alumina in 1 : 1 benzene–chloroform to give a yellow solid (0·1 g.). After recrystallisation from aqueous alcohol and vacuum-sublimation this had m. p. 130—131° alone or mixed with 5-acetamidoquinoxaline (Found: C, 64·5; H, 4·8; N, 22·6. Calc. for $C_{10}H_9ON_3$: C, 64·2; H, 4·8; N, 22·5%).

(b) *Reduction with iron powder.* (i) Iron powder (1 g.) was added gradually to a solution of the nitro-compound (I) (0·95 g.) in boiling acetic acid (10 ml.) and the solution refluxed for ½ hr., then hydrolysed, neutralised, and extracted with chloroform. Evaporation of the extract gave a black tar which was acetylated. Chromatography of the product gave 2′-*methylglyoxalino*(4′ : 5′-5 : 6)*quinoxaline* (0·25 g., 31%), which after vacuum-sublimation had m. p. 249—249·5° (Found: C, 66·0; H, 4·0; N, 30·1. $C_{10}H_8N_4$ requires C, 65·2; H, 4·3; N, 30·4%).

(ii) The reduction product, obtained as in (i), was chromatographed in chloroform–benzene (1 : 1) on alumina. A colourless band (a), faintly yellow in solution, came through rapidly, followed by a bright green fluorescent band (b) which gave a brown solution. Evaporation of the solution (a) gave the glyoxaline (II) (0·14 g., 16%), whereas (b) gave a very dark red amorphous solid, presumed to be the diamine (III) (0·2 g., 36%).

Phenanthraquinone (0·15 g.) in hot acetic acid (1 ml.) was warmed with the diamine (0·14 g.) in ethanol (1 ml.), then poured into water; the yellow 1 : 2-3 : 4-*dibenzopyrazino*(2′ : 3′-6 : 7)-*phenazine* (IV), recrystallised from nitromethane, had m. p. >300° (0·2 g., 80%) (Found: C, 79·1; H, 3·6; N, 16·7. $C_{22}H_{12}N_4$ requires C, 79·5; H, 3·6; N, 16·9%).

(c) *Reductive acetylation.* Iron powder (0·5 g.) was added gradually to a solution of the nitro-compound (I) (0·5 g.), acetic anhydride (3 ml.), and acetic acid (2 ml.), and the whole refluxed for 30 min. The product was chromatographed on alumina in chloroform–benzene (1 : 1) to give a pale yellow solid. Vacuum-sublimation and crystallisation from aqueous alcohol gave white needles, m. p. 232—233°, of 5 : 6-*diacetamidoquinoxaline* (0·45 g., 83%) (Found: C, 58·4; H, 5·1; N, 22·9. $C_{12}H_{12}O_2N_4$ requires C, 59·0; H, 4·9; N, 22·9%). Attempts to hydrolyse this material failed. After being heated for 30 min. with 5N-hydrochloric acid it was recovered. The solution in hydrochloric acid did not give a positive diazo-reaction even after prolonged boiling. Only tars resulted from hydrolysis by 5N-sodium hydroxide.

Nitration of Quinoxaline in Trifluoracetic Anhydride.—A solution of quinoxaline (1·0 g.) in trifluoracetic anhydride (12 ml.) and nitric acid (*d* 1·5; 0·5 ml.) was left for 88 hr. at room temperature. After the excess of anhydride had been distilled off, the residue was hydrolysed, neutralised, and extracted with chloroform. Evaporation of the extract and chromatography in benzene on alumina gave a yellow *hydroxynitroquinoxaline* (0·43 g., 28%), which crystallised

[7] *Org. Synth.*, 1950, **30**, 86.

from acetone in colourless prisms, m. p. 182—183° (Found: C, 50·5; H, 2·9; N, 22·5. $C_8H_5O_3N_3$ requires C, 50·3; H, 2·6; N, 22·0%).

We thank D.S.I.R. for a maintenance grant (to P. M. M.) and Dr. J. K. Landquist of Imperial Chemical Industries Limited, Dyestuffs Division, for a sample of 5-acetamidoquinoxaline.

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490. *Electrophilic Substitution. Part XI.* Nitration of Some Six-membered Nitrogen-heterocyclic Compounds in Sulphuric Acid.*

By M. J. S. DEWAR and P. M. MAITLIS.

The proportions of mononitro-derivatives formed from quinoline and *iso*quinoline in sulphuric acid have been determined. Quinoline gave at 0° 52·3% of 5- and 47·7% of 8-nitroquinoline; *iso*quinoline gave 5- and 8-nitro*iso*quinolines in the proportions: 90·4% 5-, 9·6% 8- at 0°; 84·8% 5- and 15·2% 8- at 100°. Both reactions take place readily under mild conditions. For *iso*quinoline a value for the parameter α has been derived from the partial rate factors and has been used, together with a value for β, for predictions of the reactivities of different positions in several six-membered heterocyclic systems, giving excellent agreement with experiment. Competitive nitrations have also been carried out with quinoline–*iso*quinoline and quinoline–acridine; their significance is discussed.

PREVIOUS papers [1] of this series have described electrophilic substitution of various aromatic hydrocarbons. The orientation and partial rate factors were shown to follow closely the pattern predicted [2] on the basis of a simplified molecular-orbital treatment. We have extended this investigation to some simple heterocyclic systems and now describe a study of the nitration of quinoline and *iso*quinoline in sulphuric acid.

This solvent was chosen to ensure that the reactions would involve simple electrophilic substitution. It was found that quinoline gives unexpected products in acetic anhydride or with nitrogen peroxide; we have examined [3] these reactions and given reasons for believing that they involve preliminary addition of the reagent to the 1 : 2-bond of quinoline with the formation of a reactive intermediate. Additions of this type would not be expected to occur in sulphuric acid.

Many workers have described the nitration of quinoline and *iso*quinoline. The conditions used for the former were usually drastic, involving nitric acid in oleum or in hot concentrated sulphuric acid.[4] The total yields of mononitroquinolines were around 80%, and consisted of the 5- and 8-isomers in roughly equal amounts. Nitration of *iso*quinoline has been less studied; Andersag [5] and Robinson [6] have shown it to produce both 5- and 8-nitro*iso*quinoline, but the latter was not isolated and the relative proportions of the isomers were not determined.

We have examined both these reactions in some detail, under conditions such that some of the base remained unchanged (in order to avoid dinitration and other side reactions). The mononitro-fractions were isolated by fractional basification and analysed spectrophotometrically. There was no evidence for the formation of any of the other mononitroquinolines in the nitration of quinoline; less than 1% of the 3-, 6-, or 7-nitroquinoline

* Part X, preceding paper.

[1] Dewar, *J.*, 1956, 3570, 3572, 3576, 3581.
[2] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3357.
[3] Dewar and Maitlis, *J.*, 1957, 944.
[4] Claus and Kramer, *Ber.*, 1885, **18**, 1243; Noelting and Trautmann, *Ber.*, 1890, **23**, 3655; Dufton, *J.*, 1892, **61**, 783; Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1940, **62**, 1640.
[5] Andersag, "Medicine in its Chemical Aspects," Rep. Medico-chem. Res. Lab. of the I.G. Farbenind. A.-G., 1934, **2**, 361.
[6] Robinson, *J. Amer. Chem. Soc.*, 1947, **69**, 1939.

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would have been easily detected. Similarly, in the nitration product of *iso*quinoline, there were no anomalies in the spectra to indicate presence of other isomers.

Synthetic mononitroquinolines and 5-nitro*iso*quinoline, for use as spectroscopic standards, were available. Synthesis of 8-nitro*iso*quinoline has been reported by Ochiai *et al.*,[7] by nitration of *iso*quinoline *N*-oxide, separation of the two nitro-isomers, and removal of oxygen from the 8-nitro*iso*quinoline *N*-oxide. As we were unable to repeat their work, we developed an alternative procedure. We reduced 8-nitro- to 8-amino-*iso*quinoline, which had the melting point reported by Andersag.[5] The melting point of 8-nitro*iso*quinoline (72°) and its *N*-oxide (179—180°) quoted by Ochiai *et al.* are considerably lower than those found by us.; the Japanese workers were probably dealing with eutectic mixtures of the 5- and the 8-isomer. Further they failed to obtain 8-amino*iso*quinoline by reducing their 8-nitro*iso*quinoline.

We also separated the isomeric nitro*iso*quinolines by chromatography and, with sufficiently small quantities (*ca.* 50 mg.), this separation was readily visible under ultraviolet light in the dark.

Results

In the nitrations we were unable to account for more than about 90% of the starting material in terms of unchanged base and mononitro-derivatives. However, the proportions of isomers were not only independent of the initial concentration of nitric acid but remained unchanged when the mixture of mononitro-compounds produced was treated again with nitric acid in sulphuric acid. This is indicated in the Table, where in the column headed " 8-Isomer " the first two figures refer in each line to nitration with different amounts of nitric acid, and the third figure to a mixture from one of the preceding experiments after renitration.

Compound	Reaction temp.	8-Isomer (%) (± 1%)	Mean compn. of product: 5-isomer (%)	8-isomer (%)
Quinoline	0°	52·8, 51·8, 52·2	47·7 ± 1	52·3 ± 1
*iso*Quinoline	0	9·7, 9·2, 10·0	90·4 ± 1	9·6 ± 1
,, ...	100	15·1, 15·3, 15·1	84·8 ± 1	15·2 ± 1

Several attempts to follow the kinetics failed because the reactions were essentially complete in <1 min. at 0°. (Clearly the conditions of nitration used in the past for quinoline and *iso*quinoline have been unnecessarily violent.)

Competitive nitrations were also carried out between quinoline and *iso*quinoline, and between quinoline and acridine. The relative reactivities, evaluated by the method of Dewar, Mole, and Warford,[8] were: quinoline : *iso*quinoline = 1 : 24·5; quinoline : acridine = 1 : 190.

Discussion

As recently as 1950 Schofield [9] was able to state that the electrophilic substitution of heterocyclic compounds lacked a comprehensive explanation. Since then, however, considerable progress has been made, both on the experimental and on the theoretical side, and it now seems possible to begin to provide a satisfactory and comprehensive theory.

Most theoretical treatments of aromatic substitution are based on the Wheland model [10] of the transition state and in previous papers [1] of this series it has been shown that substitution in hydrocarbons can be well interpreted in such terms. In this approach it is necessary to know the relative π-electron energies of the parent aromatic compound and of the transition state; this energy difference can be estimated [2] by a simple molecular-orbital treatment. The object of the present paper is to extend this treatment to heterocyclic systems.

[7] Ochiai *et al.*, *J. Pharm. Soc. Japan*, 1945, **65**, 73; 1951, **71**, 1385; 1953, **73**, 660 (*Chem. Abs.*, 1951, **45**, 8526; 1952, **46**, 7101; 1954, **48**, 7014).
[8] Dewar, Mole, and Warford, *J.*, 1956, 3576.
[9] Schofield, *Quart. Rev.*, 1950, **4**, 382.
[10] Wheland, *J. Amer. Chem. Soc.*, 1942, **64**, 900.

The required equations have already been published.[11] The π-electron energy difference $\Delta E_\pi'$ for substitution in a heterocycle is given by:

$$\Delta E_\pi' = \Delta E_\pi - A\sum_i a_{oi}^2\alpha_i \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

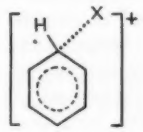
where ΔE_π is the corresponding energy difference for substitution at the corresponding position in the isoconjugate hydrocarbon, a_{oi} is the non-bonding molecular-orbital coefficient at atom i in the hydrocarbon transition state, α_i is the difference between the coulomb integral of atom i and that of carbon, and A has the value -1 for electrophilic, zero for radical, and $+1$ for nucleophilic substitution. The energy difference ΔE_π is given by:

$$\Delta E_\pi = 2\beta(a_{or} + a_{os}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where atoms r and s are those adjacent to the point of attack.

In applying equation (1) allowance must be made for the change in electronegativity of carbon atoms adjacent to heteroatoms, as the inductive effect operates along the intervening 4-bonds. It may be assumed [12] that if α is the coulomb term for a nitrogen atom, the coulomb terms of the adjacent carbon atoms are $1/3\alpha$, of the next adjacent atoms $1/9\alpha$, etc.; in practice only the nearest neighbours need be included.

In the simple Hückel treatment the appropriate value for the coulomb term (α) of nitrogen is found to lie between β and 2β (where β has its normal value of -20 kcal./mole). It was soon apparent that these values did not give agreement between the observed and the predicted values for substitutions. Further it has been shown earlier that β in

(I)  (II)

equation (2) is not the normal carbon–carbon resonance integral; the transition state (I) does not have the structure (II) postulated by Wheland but a structure intermediate between (II) and the reactants. The quantity β in equation (2) is the difference between the carbon–carbon resonance integral in the parent hydrocarbon between the point of attack and the atoms r, s and the corresponding value in the transition state. Equation (2) can thus be rewritten as:

$$\Delta E_\pi = 2\beta_X'(a_{or} + a_{os}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where β_X' is the value that β will have for a substituting agent X. β_X' will vary according to the nature of X, being numerically smaller the more reactive the substituting agent. Its value in equation (3) for nitration in acetic anhydride has been found to be -6 kcal./mole.[1] For nitration with nitric acid in sulphuric acid, a more reactive agent, β_X' should be still smaller; we have assumed a value of -4 kcal./mole.

With the usual assumption that entropy effects can be neglected, it can be shown that, for a given reagent X, the velocity constant K_r of the reaction is given by:

$$\log K_r = A_X - (\Delta E_\pi)_i/\boldsymbol{R}T \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where A_X is a constant characteristic of X, and $(\Delta E_\pi)_i$ is the change in conjugation energy of the aromatic system when atom i is removed from it. In the case of the nitration of *iso*quinoline, the difference between the change in conjugation energies at the 8- and the 5-position ($\Delta E_8 - \Delta E_5 = \delta\Delta E_\pi$) is $(p_5/p_8)_T = \exp \delta\Delta E_\pi/\boldsymbol{R}T$, where p_5 and p_8 are the partial rate factors for 5- and 8-substitution respectively. Thus, if both reactions are

[11] Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 265, 275, 283.
[12] Dewar, *J.*, 1949, 463.

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assumed complete, the experimental value for $\delta\Delta E_\pi$ can be obtained from a knowledge of the percentages of the isomers formed. Our results (9·6 ± 1% at 0°, and 15·2 ± 1% at 100°, of 8-nitro*iso*quinoline) give an average value of −1·27 ± 0·06 kcal./mole for $\delta\Delta E_\pi$. From calculations of the $\delta\Delta E_\pi$ values (see below), $\delta\Delta E_\pi$ can be shown to be $0{\cdot}032\alpha$. Thus $\alpha = -39{\cdot}7 \pm 2$ kcal./mole.

Such a value for α is not greater than the maximum value found appropriate in calculating ground-state properties of molecules by the Hückel method. The evidence therefore suggests that α has a value close to that found appropriate for calculating ground-state energies, etc., of heterocyclic compounds. This must be so if the theory is correct that the charge displacements in the transition state (I) are already close to those in the Wheland model (II); for if the charge displacements in (I) were less, α would have a numerically smaller value, just as β_X' in equation (3) is smaller numerically than the normal carbon–carbon resonance integral.

Naturally α has this value only in electrophilic substitutions where the nitrogen atom can certainly be assumed to be protonated. It has been shown by Brown [14] for free-radical, and by Chapman *et al.*[15] for electrophilic, substitution that α has values of approximately −10 and −25 kcal./mole respectively, suggesting that the ring-nitrogen atom has the greatest influence in determining substitution by electrophilic, and the least in determining substitution by free-radical, reagents, the order which would be expected.

We have adopted a value for α of −40 kcal./mole and for β_X' of −4 kcal./mole in the following calculations. Using these values and making the usual assumption that entropy effects can be neglected, we obtain remarkable agreement between predictions and experimental results. There are only two cases where the theory fails and these can be explained.

First, when the position being considered is *ortho* to the ring-nitrogen atom (as, for instance, the 8-position in quinoline and the 1-position in acridine). There are two reasons why this might be. One of the carbon atoms attached to this atom is adjacent to the nitrogen atom, therefore the electron density there and thus the coefficient will be higher than in the isoconjugate homocycle, making ΔE_π proportionately greater. A similar consideration applies to positions in the hetero-ring, but electrophilic substitution never occurs there. A second reason is that, under the conditions considered, the ring-nitrogen atom will almost invariably be protonated. Thus in attack at, say, the 8-position in quinoline, the NO_2^+ ion will approach close to a positively charged site and will be strongly hindered from substituting. Both these effects will oppose substitution *ortho* to nitrogen, and the proportion of this type of isomer will be less than expected.

The second case where the theory breaks down is for positions analogous to the 4-phenanthryl positions. It has been shown [1] that these positions are not as reactive in the hydrocarbon series as predicted, and steric hindrance in the formation of the transition state explains this for carbocyclic and heterocyclic compounds.

The results for a series of calculations on some six-membered heterocycles are listed below; the relative reactivities at different positions as calculated are compared with the experimental data. Values in parentheses are for positions where accurate value of the reactivity cannot be estimated for the reasons set out above.

$\Delta E_2 \ldots \Delta E_{10}$ refer to the values of ΔE_π for substitution at positions 2 . . . 10 in a given molecule, and are given in kcal./mole.

(1) *Pyridine.*

$$\Delta E_2 = \Delta E_4 = 2{\cdot}31\beta + 0{\cdot}333\alpha = -22{\cdot}6. \quad \Delta E_3 = 2{\cdot}31\beta + 0{\cdot}222\alpha = -18{\cdot}1.$$

Pyridine is nitrated, with great difficulty,[16] at the 3-position, as predicted.

[13] Longuet-Higgins and Coulson, *Trans. Faraday Soc.*, 1947, **43**, 87; Dewar, *J.*, 1950, 2329; D. A. Brown and Dewar, *J.*, 1953, 2406; R. D. Brown, *Quart. Rev.*, 1952, **6**, 63.

[14] R. D. Brown, *J.*, 1956, 272.

[15] Chapman and Russel-Hill, *J.*, 1956, 1563; *Chem. and Ind.*, 1954, 281, 1298; see also Chapman, *Chem. Soc. Special Publn. No.* 3, 1955, p. 155.

[16] Den Hertog and Overhoff, *Rec. Trav. chim.*, 1930, **49**, 552.

(2) *Quinoline.*

$\Delta E_2 = 2{\cdot}12\beta + 0{\cdot}500\alpha = -28{\cdot}5.$ $\Delta E_6 = 2{\cdot}12\beta + 0{\cdot}083\alpha = -11{\cdot}8.$
$\Delta E_3 = 2{\cdot}12\beta + 0{\cdot}083\alpha = -11{\cdot}8.$ $\Delta E_7 = 2{\cdot}12\beta + 0{\cdot}125\alpha = -13{\cdot}5.$
$\Delta E_4 = 1{\cdot}81\beta + 0{\cdot}364\alpha = -21{\cdot}8.$ $\Delta E_8 = 1{\cdot}81\beta + 0{\cdot}059\alpha = -9{\cdot}6.$
$\Delta E_5 = 1{\cdot}81\beta + 0{\cdot}091\alpha = -10{\cdot}9.$

The expected order of reactivity is (8) > 5 > 6 = 3 > 7 ⩾ 4 ⩾ (2). Experimentally we found roughly equal amounts of 5- and 8-nitroquinoline.

(3) iso*Quinoline.*

$\Delta E_1 = 1{\cdot}81\beta + 0{\cdot}364\alpha = -21{\cdot}8.$ $\Delta E_6 = 2{\cdot}12\beta + 0{\cdot}125\alpha = -13{\cdot}5.$
$\Delta E_3 = 2{\cdot}12\beta + 0{\cdot}125\alpha = -13{\cdot}5.$ $\Delta E_7 = 2{\cdot}12\beta + 0{\cdot}083\alpha = -11{\cdot}8.$
$\Delta E_4 = 1{\cdot}81\beta + 0{\cdot}243\alpha = -13{\cdot}0.$ $\Delta E_8 = 1{\cdot}81\beta + 0{\cdot}091\alpha = -10{\cdot}9.$
$\Delta E_5 = 1{\cdot}81\beta + 0{\cdot}059\alpha = -9{\cdot}6.$

The expected order of reactivity is 5 > 8 > 7 > 4 > 6 = (3) ⩾ (1). In practice 9·6% of 8- and 90·4% of 5-nitro*iso*quinoline are formed at 0°.

(4) *Quinoxaline.*

$\Delta E_2 = \Delta E_3 = 2{\cdot}12\beta + 0{\cdot}583\alpha = -31{\cdot}8.$ $\Delta E_6 = \Delta E_7 = 2{\cdot}12\beta + 0{\cdot}208\alpha = -16{\cdot}8.$
$\Delta E_5 = \Delta E_8 = 1{\cdot}81\beta + 0{\cdot}151\alpha = -13{\cdot}3.$

The expected order of reactivity is (5) > 6 ⩾ (2). 5-Nitroquinoxaline was found as the sole monosubstituted derivative.[17]

(5) *Quinazoline.*

$\Delta E_2 = 2{\cdot}12\beta + 0{\cdot}625\alpha = -33{\cdot}5.$ $\Delta E_6 = 2{\cdot}12\beta + 0{\cdot}125\alpha = -13{\cdot}5.$
$\Delta E_4 = 1{\cdot}81\beta + 0{\cdot}728\alpha = -36{\cdot}8.$ $\Delta E_7 = 2{\cdot}12\beta + 0{\cdot}250\alpha = -18{\cdot}5.$
$\Delta E_5 = 1{\cdot}81\beta + 0{\cdot}182\alpha = -14{\cdot}5.$ $\Delta E_8 = 1{\cdot}81\beta + 0{\cdot}091\alpha = -10{\cdot}9.$

The expected order of reactivity is (8) > 6 > 5 > 7 ⩾ (4) > (2). Elderfield *et al.*[18] and Schofield and Swain [19] report formation of 6-nitroquinazoline (56%). No other isomers have been reported.

(6) *Cinnoline.*

$\Delta E_3 = 2{\cdot}12\beta + 0{\cdot}208\alpha = -16{\cdot}8.$ $\Delta E_5 = \Delta E_8 = 1{\cdot}81\beta + 0{\cdot}121\alpha = -12{\cdot}1.$
$\Delta E_4 = 1{\cdot}81\beta + 0{\cdot}606\alpha = -31{\cdot}5.$ $\Delta E_6 = \Delta E_7 = 2{\cdot}12\beta + 0{\cdot}166\alpha = -15{\cdot}1.$

The expected order of reactivity is 5 = (8) > 6 = 7 > (3) ⩾ 4. Morley [20] has reported 5-nitrocinnoline (33%) and 8-nitrocinnoline (28%) as the sole nitration products.

(7) *Acridine* (numbering recommended by Albert, " Heterocyclic Compounds," Vol. 4, Wiley, New York, 1952).

$\Delta E_1 = 1{\cdot}57\beta + 0{\cdot}026\alpha = -7{\cdot}3.$ $\Delta E_4 = 1{\cdot}57\beta + 0{\cdot}154\alpha = -12{\cdot}4.$
$\Delta E_2 = 1{\cdot}89\beta + 0{\cdot}222\alpha = -16{\cdot}4.$ $\Delta E_5 = 1{\cdot}28\beta + 0{\cdot}400\alpha = -21{\cdot}1.$
$\Delta E_3 = 1{\cdot}89\beta + 0{\cdot}037\alpha = -9{\cdot}0.$

The expected order of reactivity is (1) > 3 > 4 > 2 ⩾ 5. Lehmstedt [21] found 3 > 1 > 4. At 50° the ratio of the isomers 3 : 4 is calculated to be 42 : 1. Lehmstedt found it to be 25 : 1.

(8) *Phenanthridine.*

$\Delta E_1 = 1{\cdot}86\beta + 0{\cdot}092\alpha = -11{\cdot}1.$ $\Delta E_6 = 2{\cdot}04\beta + 0{\cdot}167\alpha = -14{\cdot}8.$
$\Delta E_2 = 2{\cdot}18\beta + 0{\cdot}048\alpha = -10{\cdot}6.$ $\Delta E_7 = 2{\cdot}18\beta + 0{\cdot}032\alpha = -10{\cdot}0.$
$\Delta E_3 = 2{\cdot}04\beta + 0{\cdot}111\alpha = -12{\cdot}6.$ $\Delta E_8 = 1{\cdot}86\beta + 0{\cdot}138\alpha = -13{\cdot}0.$
$\Delta E_4 = 1{\cdot}96\beta + 0{\cdot}039\alpha = -9{\cdot}4.$ $\Delta E_9 = 1{\cdot}80\beta + 0{\cdot}516\alpha = -27{\cdot}8.$
$\Delta E_5 = 1{\cdot}96\beta + 0{\cdot}026\alpha = -8{\cdot}9.$

[17] Dewar and Maitlis, preceding paper.
[18] Elderfield, Williamson, Gensler, and Kremer, *J. Org. Chem.*, 1947, **12**, 418.
[19] Schofield and Swain, *J.*, 1949, 1367.
[20] Morley, *J.*, 1951, 1972; cf. Alford and Schofield, *J.*, 1953, 611.
[21] Lehmstedt, *Ber.*, 1938, **71**, 808.

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The expected order of reactivity is (5) > (4) > 7 > (1) > 3 > 8 > 6 ⩾ (9). The calculated percentages of isomers formed at 100° are: 8, 0·2%; 3, 0·3%; 1, 2·6%; 2, 5·2%; 7, 8·4%; 4, 26·8%; 5, 53·1%. Caldwell and Walls [22] found: 3, 3% 1, 1%; 2, 6%; 7, 11%; 4, 26%; 5, 21%.

(9) *Benzo*[f]*quinoline* (Ring Index numbering).

$\Delta E_1 = 1{\cdot}86\beta + 0{\cdot}310\alpha = -19{\cdot}8$. $\Delta E_7 = 1{\cdot}86\beta + 0{\cdot}034\alpha = -8{\cdot}8$.
$\Delta E_2 = 2{\cdot}12\beta + 0{\cdot}127\alpha = -13{\cdot}6$. $\Delta E_8 = 2{\cdot}18\beta + 0{\cdot}032\alpha = -10{\cdot}0$.
$\Delta E_3 = 2{\cdot}04\beta + 0{\cdot}375\alpha = -23{\cdot}2$. $\Delta E_9 = 2{\cdot}04\beta + 0{\cdot}042\alpha = -9{\cdot}8$.
$\Delta E_5 = 1{\cdot}80\beta + 0{\cdot}022\alpha = -8{\cdot}1$. $\Delta E_{10} = 1{\cdot}96\beta + 0{\cdot}026\alpha = -8{\cdot}9$.
$\Delta E_6 = 1{\cdot}80\beta + 0{\cdot}129\alpha = -12{\cdot}4$.

The expected order of reactivity is (5) > 7 > (10) > 9 > 8 > 6 > 2 ⩾ (1) ⩾ (3). The order of reactivity found was 7 > 10 > 9. The calculated ratio of isomers, 7 : 9 at 0° is 6·7 : 1. Ochiai *et al.*[23] found it to be 5·7 : 1; Boehm [24] found it as 4·8 : 1.

(10) *Phenazine.*

$\Delta E_1 = 1{\cdot}57\beta + 0{\cdot}180\alpha = -13{\cdot}5$. $\Delta E_2 = 1{\cdot}89\beta + 0{\cdot}259\alpha = -17{\cdot}9$.

The 1- would be expected to be formed in preference to the 2-isomer. Maffei and Aymon [25] reported finding the 1-isomer as the sole mono-substituted product.

(11) *Benzo*[c]*cinnoline* (Ring Index numbering).

$\Delta E_1 = 1{\cdot}96\beta + 0{\cdot}051\alpha = -10{\cdot}0$. $\Delta E_3 = 2{\cdot}18\beta + 0{\cdot}063\alpha = -11{\cdot}3$.
$\Delta E_2 = 2{\cdot}04\beta + 0{\cdot}222\alpha = -17{\cdot}0$. $\Delta E_4 = 1{\cdot}86\beta + 0{\cdot}184\alpha = -14{\cdot}8$.

The expected order of reactivity is (1) > 3 > (4) > 2. Smith and Ruby [26] found 1-nitrobenzo[*c*]cinnoline (57%) together with another substance which they considered to be the 3-isomer (12%).

Except in this paper, no attempt has been made to compare the relative reactivities of two heterocycles. From our results the ratio of the partial rate factors $K_{5\text{-nitro}iso\text{quinoline}} : K_{5\text{-nitroquinoline}}$ was calculated [8] to be 46·4 : 1. From the above calculations $\Delta E_{\pi(5\text{-nitroquinoline})} - \Delta E_{\pi(5\text{-nitro}iso\text{quinoline})}$ is found to be −1·3 kcal./mole. This gives a theoretical value for the ratio of these partial rate factors of 10·5 : 1.

An attempt was also made to see whether the allowance to be made for positions *ortho* to the nitrogen atom was constant, by comparing the reactivities of the 8-position in quinoline with those for the 1-position in acridine. Using the figures obtained by Lehmstedt [21] for the ratios of mononitroacridines formed in nitration, we arrived at a value of 27·5 : 1 for the ratio of the partial rate factors, 8-nitroquinoline : 1-nitroacridine. The calculated value is 79 : 1.

In both these cases, having regard to the difficulty of obtaining accurate experimental data, it must be concluded that the correspondence between the experimental facts and theory is of the correct order.

Experimental

Microanalyses were by the Microanalytical Laboratory, Imperial College of Science and Technology, London.

Materials.—*iso*Quinoline (from B.D.H.) was recrystallised. Commercial quinoline of " puriss." grade was used for some experiments; this contained 5·9% of *iso*quinoline, estimated as previously described.[27] Allowance could be made for this impurity since nitro*iso*quinolines can easily be separated from nitroquinolines by chromatography. In the quinoline–acridine

[22] Caldwell and Walls, *J.*, 1952, 2156.
[23] Ochiai and Tamura, *J. Pharm. Soc. Japan*, 1952, **72**, 985 (*Chem. Abs.* 1953, **47**, 12385).
[24] Boehm, *Roczniki Chem.*, 1950, **24**, 128.
[25] Maffei and Aymon, *Gazzetta*, 1954, **84**, 667.
[26] Smith and Ruby, *J. Amer. Chem. Soc.*, 1954, **76**, 5807.
[27] Maitlis, *Analyst*, 1957, **82**, 135.

competitive nitration, synthetic quinoline was used. The nitric acid was commercial fuming nitric acid (*d* 1·5; HNO_3 97%); sulphuric acid (*d* 1·84) was used as a medium for all nitrations. Solvents for chromatography were distilled before use. Light petroleum was of b. p. 40—60° unless otherwise stated.

6- and 8-Nitroquinoline were available commercially; the 5- and the 7-isomer were prepared by Bradford, Elliot, and Rowe's method.[28] 5-Nitro*iso*quinoline (m. p. 110·5—111·5°) was obtained by repeated recrystallisation (from aqueous alcohol) of the nitration product from *iso*quinoline. All the isomers were crystallised to constant m. p. and vacuum-sublimed before use. Spectra were measured on a Unicam S.P.500 spectrophotometer; *cyclo*hexane (spectroscopically pure) was used as solvent.

8-*Nitroisoquinoline*.—Nitric acid (6·2 ml.) was added to a solution of *iso*quinoline *N*-oxide [7] (18 g.) in sulphuric acid (80 ml.) and the mixture heated for 1 hr. at 95°, cooled, and poured on ice. The nitro*iso*quinoline *N*-oxides were isolated with chloroform and recrystallised from acetone, to give 5-nitro*iso*quinoline *N*-oxide (13 g., 64%), which after recrystallisation from nitromethane had m. p. 220—221° (lit., 220°). The mother-liquors, on evaporation, left a black tar, which was chromatographed on alumina to give fractions (*a*) *iso*quinoline *N*-oxide (2·2 g.) and (*b*) a yellow solid (2·7 g.) which on fractional crystallisation from acetone gave 8-nitro*iso*quinoline *N*-oxide (1·4 g., 7%), m. p. 188—189° (Found: C, 57·1; H, 3·2; N, 14·9. Calc. for $C_9H_6O_3N_2$: C, 56·8; H, 3·2; N, 14·7%). A solution of the *N*-oxide (0·5 g.) in phosphorus trichloride (7 ml.) was boiled under reflux for 30 min.; water was then added and the 8-nitro*iso*quinoline isolated with chloroform, chromatographed, and crystallised from ether–light petroleum to m. p. 87—87·5° (yield 65%) (Found: C, 61·9; H, 3·3; N, 15·8. Calc. for $C_9H_6O_2N_2$: C, 62·1; H, 3·4; N, 16·1%).

Reduction of the nitro-compound with hydrazine hydrate and palladized charcoal (cf. Dewar and Mole [29]) gave 8-amino*iso*quinoline (60%), yellow needles (from light petroleum), m. p. 170—171° (lit.,[5] 171°). 5-Nitro*iso*quinoline was prepared from the *N*-oxide in an analogous manner in 52% yield.

Nitrations of Quinoline and iso*Quinoline*.—The reactions were carried out in sulphuric acid, a solution of nitric acid being added gradually to one of the base. After 30 min. the solutions were poured on ice. The mononitro-fraction was separated by partial basification (at pH 2·1 for quinoline; at pH 2·5 for *iso*quinoline) from unchanged base and analysed spectroscopically. The results were evaluated by Dewar and Urch's method,[30] which is highly accurate for two-component mixtures (in this case better than ±1%). In the quinoline series, both the 5- and the 8-nitroquinoline have peaks around 300 mμ and troughs at about 250 mμ, whereas the 3-, 6-, and 7-isomer have considerable peaks at 250 mμ; this would make it possible to detect less than 1% of any of these isomers. Further no anomalies could be found in the spectra of any of the mixtures such as would be caused by the presence of a third isomer. The peaks of the spectra are given (log ε values in parentheses):

Quinoline	Max.
3-Nitro ...	252 mμ (4·58), 298 mμ (4·14)
5-Nitro ...	305 mμ (3·80)
6-Nitro ...	249 mμ (4·40), 257 mμ (4·34), 286 mμ (3·98)
7-Nitro ...	249 mμ (4·35), 257 mμ (4·28), 286 mμ (3·96)
8-Nitro ...	275 mμ (3·74), 301 mμ (3·54), 315 mμ (3·52)

*iso*Quinoline	Max.
5-Nitro- ...	235 mμ (4·12), 333 mμ (3·70)
8-Nitro ...	235 mμ (4·17), 292 mμ (3·56), 328 mμ (3·54)

Check experiments were also carried out in which the mixtures of nitro-compounds were re-treated with the nitration mixture; in each case at least 95% of the material was recovered. The nitration data are summarised in the following Table (Q = quinoline; I = *iso*quinoline).

Summary of nitration experiments.

Base	Temp.	Base (g.)	Solution (ml.)	10% HNO_3 (ml.)	Base recovered (mol. %)	Nitro-isomers isolated (mol. %)
Q	0°	1·738	20	2·0	69	24
Q	0	1·738	20	4·0	44	46
I	0	5·120	30	7·0	45	38
I	0	5·120	30	15·0	2	80
I	100	5·120	30	7·0	52	36
I	100	5·120	30	15·0	15	75

[28] Bradford, Elliot, and Rowe, *J.*, 1947, 442.
[29] Dewar and Mole, *J.*, 1956, 2556.
[30] Dewar and Urch, *J.*, 1957, 345.

Competitive Nitration of Quinoline and iso*Quinoline.*—A mixture of *iso*quinoline (4·452 g.) and quinoline (8·500 g.) (both corr. for the presence of 5·9% of *iso*quinoline in the quinoline) was dissolved in sulphuric acid and the volume made up to 90 ml. (*A*). A solution of nitric acid in sulphuric acid (10% v/v; 2·7 ml.) was added to solution (*A*) (30 ml.), and the mixture was kept at 0° with stirring for 30 min., then worked up in the usual way, partial basification being carried out at pH 2·5. The solid residue of mixed nitroquinolines and nitro*iso*quinolines was chromatographed. A second parallel nitration was carried out. Results were:

(*a*) nitroquinolines 0·092 g.; nitro*iso*quinolines 0·904 g.

(*b*) nitroquinolines 0·088 g.; nitro*iso*quinolines 0·884 g.

Competitive Nitration of Quinoline and Acridine.—A mixture of pure synthetic quinoline (7·042 g.) and acridine (1·176 g.) was dissolved in concentrated sulphuric acid (15 ml.); to this was added nitric acid in sulphuric acid (10% v/v; 2·0 ml.) with stirring at 0°. The whole was left at this temperature for 30 min., then poured on ice. By the usual procedure of partial basification a solid fraction was obtained not containing any quinoline. This was chromatographed in benzene–light petroleum (1 : 1) on alumina. The material soon separated into two bands, the first fluorescent, but with a small dark patch in it visible under ultraviolet light (acridine, 0·755 g., containing a small amount of nitroquinolines). It was not possible to separate the mixture of nitroquinoline and acridine, and it was therefore hoped that it would be possible to analyse the mixture microanalytically, since the percentages of carbon in the two constituents were so different. Unfortunately the results were not very consistent and an average value (C, 84·2%) had to be used, corresponding to 11·8% of nitroquinolines (0·033 g.) in the mixture.

We thank D.S.I.R. for a maintenance grant (to P. M. M.), and Kodak Ltd. for a gift of synthetic quinoline.

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491. *The Homolytic Addition of Chloroacetone to Olefins.*

By R. L. HUANG.

Chloroacetone adds homolytically to dec-1-ene to give 3-chlorotridecan-2-one, whose structure has been established by degradation. Addition proceeds less effectively with allylbenzene and ethyl undec-10-enoate, and fails with allylacetone, *cyclo*hexene, and ethyl crotonate. A chain mechanism is proposed.

CHLOROACETONE, under catalysis by benzoyl or *tert.*-butyl peroxide, adds homolytically to dec-1-ene, to give the chloro-ketone (I), whose constitution is established by the following evidence. (*a*) Reaction with thiourea gave the aminothiazole (II), characterised as the acetyl derivative, showing the adduct to be an α-chloro-ketone.[1] (*b*) Treatment with

$C_{10}H_{21}\cdot CHCl\cdot COMe$ (I) $\quad$ $C_{10}H_{21}\cdot C(=CMe)\cdot S\cdot C(=NH)\cdot NH_2$ (II) $\quad$ $C_{10}H_{21}\cdot CH(OH)\cdot COMe$ (III) $\quad$ $Ph\cdot CO\cdot CH(OH)\cdot[CH_2]_3\cdot CO_2H$ (IV)

potassium hydroxide readily yielded the hydroxy-ketone (III) which was oxidised by potassium permanganate to decanoic acid. [Oxidation to decanoic rather than undecanoic acid might seem unexpected, but finds an analogy in a similar oxidation of the hydroxy-ketone (IV) to succinic acid in over 50% yield.[2]] The following chain mechanism for the addition is proposed:

(1) $CH_3\cdot CO\cdot CH_2Cl + R\cdot$ (from the peroxide) $\longrightarrow CH_3\cdot CO\cdot CHCl\cdot + RH$

(2) $CH_3\cdot CO\cdot CHCl\cdot + C_8H_{17}\cdot CH{=}CH_2 \longrightarrow C_8H_{17}\cdot\dot{C}H\cdot CH_2\cdot CHCl\cdot COMe$ (V) . (Initiation)

(3) $(V) + CH_3\cdot CO\cdot CH_2Cl \longrightarrow (I) + CH_3\cdot CO\cdot CHCl\cdot$ . . . (Propagation)

[1] Traumann, *Annalen*, 1888, **249**, 38; King and Hlavacek, *J. Amer. Chem. Soc.*, 1950, **72**, 3722; cf. Huang, *J.*, 1957, 1342.

[2] Huang and Williams, unpublished work.

That the initiating radical is $CH_3{\cdot}CO{\cdot}CHCl{\cdot}$ (reaction 1) and not $CH_3{\cdot}CO{\cdot}CH_2{\cdot}$ follows from the fact that the adduct is an α- and not a γ-chloro-ketone. This confirms previous findings that a hydrogen atom is more susceptible to attack by free radicals than is a chlorine atom, as in the cases of chloroacetic acid and chloroalkanes reported by Kharasch and his co-workers.[3] The structure of the adduct also shows that addition takes place initially at the end of the chain, to give the more resonance-stabilised intermediate radical (V), and thus conforms to the usual pattern of addition of other substances, *e.g.*, aliphatic aldehydes [4] and halogenated methanes,[5] to terminal double bonds, as that in oct-1-ene.

One marked departure from these known homolytic additions, however, is the relatively large quantities of catalyst required for any reasonable yield of the adduct. Thus 20 moles % of either peroxide gave only a 30% yield, the highest obtained. The yield dropped to 14—16% when only 10 moles % of benzoyl peroxide were used, under varied conditions, and moreover in each case at least a third of the olefin did not enter reaction despite presence of a large excess of chloroacetone. In all cases, considerable quantities of polymeric products were formed, although none of the " dimer " of chloroacetone (VI) was encountered. These results seem best explained by inefficient propagation rather than inadequate initiation, with some of the intermediate radicals undergoing telomerisation and dimerisation, instead of carrying on the chain.

In surveying the scope of this reaction, addition to different types of olefins was studied, under the optimum conditions found above. *cyclo*Hexene gave very little if any of the adduct, some polymeric products, and in contrast to dec-1-ene, much unchanged olefin, indicating inadequate propagation but excluding telomerisation as a major chain-breaking process. It is of interest that aliphatic aldehydes (*e.g.*, butanal) also add sluggishly to *cyclo*hexene.[4] Ethyl crotonate behaved similarly; although with this olefin the ready addition of butanal (77% yield) [6] presents a striking contrast.

To explore possible applications in synthesis the addition of chloroacetone to substances containing a terminal double bond and another functional group was investigated. Allylbenzene and ethyl undec-10-enoate afforded only modest yields of the adducts (VII) and (VIII), while allylacetone gave none of the expected (IX) under a variety of conditions. In contrast addition of butanal to these substances gave fair yields of the adducts (X), (XI), and (XII) respectively, although no attempts were made to ascertain the optimum conditions.

$(CH_3{\cdot}CO{\cdot}CHCl{\cdot})_2$ (VI) $\quad Ph{\cdot}[CH_2]_3{\cdot}R$ (VII) R = $\cdot CHCl{\cdot}COMe$, (X) R = $\cdot CO{\cdot}C_3H_7$ $\quad EtO_2C{\cdot}[CH_2]_{10}{\cdot}R$ (VIII) R = $\cdot CHCl{\cdot}COMe$, (XI) R = $\cdot CO{\cdot}C_3H_7$ $\quad Me{\cdot}CO{\cdot}[CH_2]_4{\cdot}R$ (IX) R = $\cdot CHCl{\cdot}COMe$, (XII) R = $\cdot CO{\cdot}C_3H_7$

Experimental

Addition of Chloroacetone to Dec-1-ene.—(*a*) Benzoyl peroxide (2·9 g., 0·012 mole) was added in 4 portions during 6 hr. to a mixture of dec-1-ene (n_D^{21} 1·4201; 8·9 g., 0·064 mole) and chloroacetone (46 g., 0·48 mole) at 70—75° under nitrogen. Heating was continued for 3 hr. more, for the last hr. at 85—90°. There was some evolution of hydrogen chloride during the last stages of heating. Excess of chloroacetone was removed under reduced pressure (b. p. 52°/70 mm.), and the product diluted with ether and washed five times with 5% aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and concentrated. Distillation then gave (i) a forerun, from which benzoic acid separated (*ca.* 0·2 g.; m. p. and mixed m. p.); (ii) *3-chlorotridecan-2-one*, b. p. 102°/1 mm., $n_D^{21\cdot5}$ 1·4546 (4·8 g., 30%); and (iii) a residue (4·0 g.), which did not distil at 175° (bath)/1 mm. Further distillation of fraction (ii) gave a pure sample, b. p. 100° (bath)/0·5 mm., n_D^{20} 1·4521 (Found: C, 67·4; H, 10·7; Cl, 15·2. $C_{13}H_{25}OCl$ requires C, 67·1; H, 10·75; Cl, 15·3%). With semicarbazide and sodium acetate in aqueous ethanol it gave low yields of a solid, m. p. *ca.* 150—160°, which appeared to be a mixture of semicarbazones.

[3] Kharasch, Urry, and Jensen, *J. Amer. Chem. Soc.*, 1945, **67**, 1626; *J. Org. Chem.*, 1945, **10**, 386; Kharasch and Büchi, *J. Amer. Chem. Soc.*, 1951, **73**, 632.
[4] Kharasch, Urry, and Kuderna, *J. Org. Chem.*, 1949, **14**, 248.
[5] Kharasch, Jensen, and Urry, *J. Amer. Chem. Soc.*, 1947, **69**, 1100.
[6] Huang, *J.*, 1956, 1749.

(*b*) Under the same conditions but with 10 mole % of benzoyl peroxide and a 5 mole excess of chloroacetone, dec-1-ene (21 g.) gave a product which on distillation yielded : (i) unchanged decene, b. p. 48°/50 mm. (6·5 g.); (ii) material of b. p. 108—113°/4 mm. (*ca.* 1·5 g.); (iii) 3-chlorotridecan-2-one, b. p. 113°/4 mm., n_D^{20} 1·4546 (3·7 g., 14% yield, calc. on decene consumed); and (iv) a residue (7 g.).

(*c*) Using the same quantities of reactants as in (*b*) but adding the catalyst in 3 portions during 20 hr., and heating the mixture at 70° for a total of 26 hr., gave a 16% yield of adduct.

(*d*) Dec-1-ene (14 g., 0·10 mole), chloroacetone (56 g., 0·60 mole), and di-*tert.*-butyl peroxide (2·9 g., 0·02 mole) were heated together at 125—130° under reflux in nitrogen for 44 hr. After removal of the volatile fractions and of excess of chloroacetone, the product on distillation gave 3-chlorotridecan-2-one, b. p. 106—108°/*ca.* 2 mm., $n_D^{21\cdot5}$ 1·4508 (7·0 g., 30%). There was an undistillable residue (6·8 g.).

Reaction with Thiourea.—The above adduct (1·0 g.) and thiourea (0·33 g.) were refluxed in absolute ethanol (*ca.* 10 c.c.) for 20 hr. Most of the ethanol was distilled off and the residue treated with concentrated aqueous ammonia (20 c.c.), and the oil which separated taken up in ether, washed with water, dried, and after removal of the solvent heated with acetic anhydride (10 c.c.) and acetic acid (1 c.c.) at 90° for 6 hr., and boiled for 5 min. The solution was poured on ice, and the solid which separated was recrystallised from aqueous ethanol, then from methanol, giving *2-acetamido-5-decyl-4-methylthiazole*, needles, m. p. 75° (0·8 g.) (Found : N, 9·3; S, 10·9. $C_{16}H_{28}ON_2S$ requires N, 9·4; S, 10·8%).

Degradation.—(*a*) 3-Chlorotridecan-2-one (1 g.) was unaffected by potassium acetate (1 g.) in acetic acid (10 c.c.) at 80° for 16 hr.

(*b*) The chloro-ketone (2·6 g.) in absolute ethanol (*ca.* 5 c.c.) was mixed with potassium hydroxide (0·75 g.) in the same solvent (10 c.c.). The mixture became warm, darkened, and soon deposited a yellow precipitate. After 24 hr. at room temperature, acetic acid (0·5 c.c.) was added, the solid filtered off, and the filtrate concentrated by distillation, then poured on ice, and extracted with ether. After being washed with aqueous sodium hydrogen carbonate and water, dried, and freed from solvent, the product was distilled, to give two fractions of the same refractive index, n_D^{21} 1·4481, b. p. 100—110° (bath)/0·4 mm. (1·5 g., 68%). A sample of this gave a good yield of *3-hydroxytridecan-2-one semicarbazone*, needles (from aqueous ethanol), m. p. 173—174° (Found : C, 62·0; H, 10·65; N, 16·0. $C_{14}H_{29}O_2N_3$ requires C, 61·95; H, 10·8; N, 15·5%).

The above hydroxy-ketone (1·0 g.) in acetone (20 c.c.) was treated [7] with potassium permanganate (1·6 g.) and magnesium sulphate (0·6 g.) in water (20 c.c.). A slight rise in temperature was noted. The mixture was heated under reflux for 90 min., then filtered, and the colourless filtrate concentrated on the steam-bath to *ca.* 25 c.c. 20% Aqueous sodium carbonate (5 c.c.) was added, and the solution washed with ether, then acidified with 5N-sulphuric acid, and the oil which separated was taken up in ether and dried. On removal of ether, the oily acid obtained was converted *via* the acid chloride into the decananilide, needles (from aqueous ethanol), m. p. and mixed m. p. 69—70° (0·5 g.) (Found : N, 5·44. Calc. for $C_{16}H_{25}ON$: N, 5·66%). When mixed with a sample of undecananilide of m. p. 68°, it melted at 59—62°.

Other Addition Reactions of Chloroacetone.—(a) *Ethyl undec-10-enoate.* This ester (21 g., 0·10 mole; n_D^{22} 1·4375) with chloroacetone (46 g., 0·50 mole) and benzoyl peroxide (2·4 g., 0·01 mole) gave, by procedure (a), fractions : (i) unchanged ester, b. p. 83—84°/1 mm., n_D^{22} 1·4393 (10·6 g.); (ii) a pale yellow liquid, b. p. *ca.* 158°/1 mm., n_D^{23} 1·4615 (1·5 g.); (iii) undistillable residue (10·0 g.). Fraction (ii) on further distillation gave *ethyl 12-chloro-13-oxotetradecanoate*, b. p. 150° (bath)/0·5 mm., n_D^{21} 1·4612 (Found : Cl, 11·2. $C_{16}H_{29}O_3Cl$ requires Cl, 11·6%).

(b) *Allylbenzene.* Allylbenzene (12 g., 0·10 mole), chloroacetone (58 g., 0·63 mole), and benzoyl peroxide (4·8 g., 0·02 mole) after 20 hr. at 65° and 1 hr. at 85° gave, on fractionation, *3-chloro-6-phenylhexan-2-one*, b. p. 97—102°/1 mm. (1·0 g.), n_D^{20} 1·5258 (Found : Cl, 16·9. $C_{12}H_{15}OCl$ requires Cl, 16·8%).

(c) *Allylacetone* (n_D^{21} 1·4193; see Schechter *et al.*[8]). No adduct was obtained by using (*a*) benzoyl peroxide (10 or 20 mole%) or (*b*) *tert.*-butyl peroxide.

Addition of Butanal to Ethyl Undec-10-enoate.—The ester (24 g., 0·11 mole), butanal (40 g., 0·55 mole), and benzoyl peroxide (1·5 g., 0·006 mole) were refluxed under nitrogen for 20 hr.

[7] Cf. Clarke and Howes, *J.*, 1956, 1152.
[8] Schechter, Green, and La Forge, *J. Amer. Chem. Soc.*, 1949, **71**, 3165.

After removal of excess of butanal by distillation, the product was taken up in ether and washed with aqueous sodium hydrogen carbonate, dried, and distilled. Unchanged ester (4 g.) was thus recovered. The residue slowly deposited *ethyl 12-oxopentadecanoate*, rods (9·5 g., 35%), which after recrystallisation from 90% ethanol had m. p. 41° (Found : C, 72·0; H, 11·2. $C_{17}H_{32}O_3$ requires C, 71·8; H, 11·3%). The semicarbazone, needles (from aqueous ethanol), melted at 69—71° (Found : N, 12·0. $C_{18}H_{35}O_3N_3$ requires N, 12·3%). Ultraviolet irradiation (Towers lamp) of the same mixture (peroxide being omitted) gave small quantities of the adduct (0·8 g.) after 23 hr., most of the reactants being recovered.

The above product (0·6 g.) was hydrolysed by potassium carbonate (1 g.) in boiling 50% ethanol (10 c.c.) for 4 hr., giving *12-oxopentadecanoic acid*, needles (from ethanol), m. p. 127° (Found : C, 69·9; H, 10·8. $C_{15}H_{28}O_3$ requires C, 70·3; H, 11·0%).

Addition of Butanal to Allylacetone.—Allylacetone (5·0 g., 0·05 mole), butanal (22 g., 0·30 mole), and benzoyl peroxide (1·1 g., 0·005 mole) by the same procedure gave *decane-2 : 7-dione*, b. p. 80—82°/1 mm., n_D^{18} 1·4415 (4·5 g., 53%) (Found : C, 70·0; H, 10·6. $C_{10}H_{18}O_2$ requires C, 70·5; H, 10·7%). The bis-semicarbazone, obtained by refluxing the diketone (0·6 g.) with semicarbazide hydrochloride (1·5 g.) and sodium acetate (1·5 g.) in 50% ethanol (20 c.c.) for 20 min., was crystallised from aqueous ethanol, then from methanol, and had m. p. 166—168° (Found : N, 28·9. $C_{12}H_{24}N_6$ requires N, 29·5%).

Addition of Butanal to Allylbenzene.—Allylbenzene (17 g., 0·15 mole), butanal (67 g., 0·9 mole), and benzoyl peroxide (2·4 g., 0·01 mole) by the same procedure gave (i) unchanged allylbenzene (12 g.) and (ii) *1-phenylheptan-4-one*, b. p. 111°/2 mm. (4·5 g., 56% yield calc. on allylbenzene consumed), n_D^{22} 14970 (Found : C, 82·0; H, 9·7. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%). Attempts to prepare solid derivatives with semicarbazide and 2 : 4-dinitrophenylhydrazine were unsuccessful.

Microanalyses were by Dr. W. Zimmermann, Melbourne.

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492. *Ring–Chain Tautomerism in the Acid Esters of Pyridine-2 : 3-dicarboxylic Acid.*

By J. KENYON and KUMAR THAKER.

Pyridine-2 : 3-dicarboxylic anhydride and methanol combine exothermally in equimolecular proportions at room temperature, to form a viscous compound which is probably a hemi-acetal. Within an hour at room temperature this changes spontaneously and completely into crystalline methyl 2-carboxypyridine-3-carboxylate which in turn changes to the isomeric methyl 3-carboxypyridine-2-carboxylate when its solutions are heated; conversely methyl 3-carboxypyridine-2-carboxylate is smoothly re-converted into methyl 2-carboxypyridine-3-carboxylate at 150°. The viscous compound is hygroscopic and forms a stable crystalline hydrate. Both the viscous compound and its crystalline hydrate with diazomethane readily give dimethyl pyridine-2 : 3-dicarboxylate.

(+)-*sec.*-Butyl 2-carboxypyridine-3-carboxylate, when heated in ethyl acetate, is converted into (+)-*sec.*-butyl 3-carboxypyridine-2-carboxylate without significant loss of molecular dissymmetry. (−)-*sec.*-Butyl 3-carboxypyridine-2-carboxylate is smoothly decarboxylated at 160° to optically pure (−)-*sec.*-butyl nicotinate.

BY heating a mixture of pyridine-2 : 3-carboxylic anhydride and methanol for several hours, Kirpal [1] obtained a methyl carboxypyridinecarboxylate which, since it gave methyl nicotinate on decarboxylation, he believed to be methyl 2-carboxypyridine-3-carboxylate (V). Later he showed [2] that by the successive action of ammonia, hypobromite, and heat this compound gave 2-aminopyridine; accordingly he concluded that the compound was

[1] Kirpal, *Monatsh.*, 1899, **20**, 766.
[2] *Idem, ibid.*, 1900, **21**, 957.

the isomer, methyl 3-carboxypyridine-2-carboxylate (VI). Still later [3] he found that the reaction between pyridine-2 : 3-dicarboxylic anhydride and methanol afforded not only the 2-methyl ester but also, in much smaller proportion, the 3-methyl ester, the structure of which was similarly established by its conversion into 3-aminopyridine. Kirpal showed that this 3-methyl ester, like the 2-methyl ester, when heated above its melting point lost carbon dioxide and yielded methyl nicotinate (VII).

To account for the unexpected migration of a methyl group involved in the production of methyl nicotinate from methyl 3-carboxypyridine-2-carboxylate Kirpal made the highly improbable suggestion of the intermediate formation of dimethyl pyridine-2 : 3-dicarboxylate, though he was unable to detect it. It is now shown that methyl 3-carboxypyridine-2-carboxylate is smoothly transformed, at temperatures below those at which decarboxylation occurs, into methyl 2-carboxypyridine-3-carboxylate, *i.e.*, a compound containing the esterfied group in the appropriate position and the free carboxyl group favourably disposed for smooth decarboxylation.

By conductivity measurements Kirpal [3] showed that the 2-methyl ester, which is not hydrolysed in even very dilute aqueous solution, is a stronger acid than the isomeric 3-methyl ester and pointed out that since the 2-methyl ester had been obtained in yields exceeding 80% pyridine-2 : 3-dicarboxylic anhydride does not obey Wegscheider's rule [4] that esterification of anhydrides of unsymmetrical dicarboxylic acids always occurs at the stronger carboxylic group.

When a mixture of pyridine-2 : 3-dicarboxylic anhydride and methanol is heated both the 2- and the 3-methyl carboxypyridinecarboxylates are produced, the proportion of the former increasing as the heating is prolonged. Further, the pure 3-methyl ester is almost completely converted into the 2-methyl ester when its solution in ethyl acetate is boiled for an hour—a conversion doubtless facilitated by the more sparing solubility of the 2-ester which separates from the solution preferentially.

Thus it appears that the esterification of pyridine-2 : 3-dicarboxylic anhydride by methanol affords no exception to Wegscheider's rule and that Kirpal's isolation of the 2-methyl ester in such a preponderating proportion, and his earlier failure to find the 3-methyl ester, were a direct consequence of prolonged heating.

Pyridine-2 : 3-dicarboxylic anhydride and methanol in molecular proportions at room temperature form a viscous liquid (I) which, in turn, combines with water, even from the atmosphere, to give a crystalline monohydrate (IV). There is a marked difference in reactivity between (I) and its crystalline hydrate : the freshly prepared acetal (I), shaken with cold water, gives a clear solution which almost instantly deposits pyridine-2 : 3-dicarboxylic acid (III) quantitatively; after being kept for some 30 minutes and provided it has not already solidified, a solution of the acetal in cold water deposits almost pure methyl 2-carboxypyridine-3-carboxylate : if the acetal has spontaneously solidified (an exothermic process), the product can be separated by crystallisation into the 2- and the 3-methyl carboxypyridinecarboxylates.

It is highly improbable that the pyridinedicarboxylic acid obtained from the acetal by the action of an excess of cold water is formed by hydrolysis of initially liberated pyridine-2 : 3-dicarboxylic anhydride since this compound is unaffected by cold water. It seems more likely that the anhydride is first set free in the reactive hydroxylated form (II) which immediately rearranges to the acid (III).

It is curious that compound (IV) does not lose the elements of methanol as does the freshly prepared acetal when mixed with an excess of water, for it yields the isomeric 3-methyl ester (V).

Compound (I) must begin to undergo some kind of isomeric change almost immediately after formation, for even after only 5 minutes it no longer yields pyridinedicarboxylic acid when shaken with water : the solution gives methyl 2-carboxypyridine-3-carboxylate.

[3] Kirpal, *Monatsh.*, 1907, **28**, 439; 1908, **29**, 227.
[4] Wegscheider, *ibid.*, 1897, **18**, 631.

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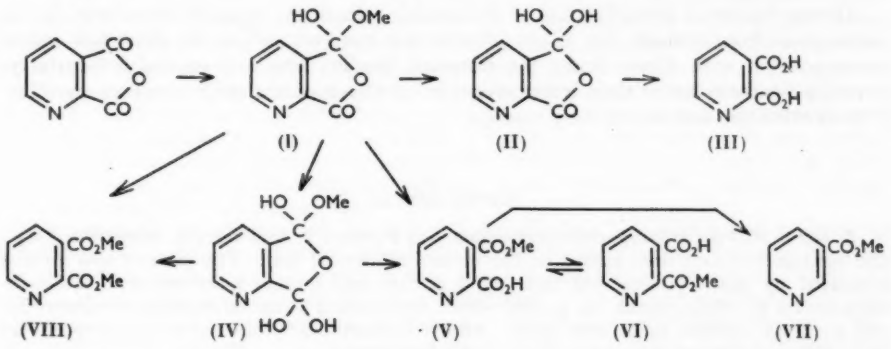
These results suggest that the first product of the combination of methanol and pyridine-2 : 3-dicarboxylic anhydride is the hemiacetal (I) which even at room temperature changes to methyl 2-carboxypyridine-3-carboxylate (V).

Recent work [5] on the ultraviolet absorption spectra of solutions of phthalic anhydrides in ethanol and non-hydroxylic solvents suggests the formation of intermediates of type (I) which isomerise gradually to alkyl hydrogen phthalates; *e.g.*, it is stated that a solution of


HO OMe
HO OH
CO
CO
CO

intramolecular is afforded by the observation that heating methyl 2-carboxypyridine-3-carboxylate in *sec.*-butyl alcohol gives only methyl 3-carboxypyridine-2-carboxylate.

(+)-*sec.*-Butyl 2-carboxypyridine-3-carboxylate and (−)-*sec.*-butyl 3-carboxypyridine-2-carboxylate each yields a brucine salt of m. p. 186°. After the second of these has been kept at its m. p. for a short time, hydrochloric acid liberates *sec.*-butyl 2-carboxypyridine-3-carboxylate, m. p. 131°: thus the second brucine salt is converted into the first during melting.

During fractional crystallisation of the brucine salts of *sec.*-butyl 2-carboxypyridine-3-carboxylate from acetone one of the filtrates was concentrated *on the steam-bath* before decomposition with dilute acid; the liberated product was (−)-*sec.*-butyl 3-carboxypyridine-2-carboxylate: thus interconversion of the isomeric acid esters of pyridine-2 : 3-dicarboxylic acid occurs very readily.

Experimental

2- and 3-Methyl Carboxypyridinecarboxylate.—(i) Pyridine-2 : 3-carboxylic anhydride (7·6 g.) and methanol (5 c.c.) were heated on the steam-bath for 40 min. The product (6·5 g.) was separated by one crystallisation from ethyl acetate into methyl 2-carboxypyridine-3-carboxylate (4·1 g., 45%), plates, m. p. 102—103°, and methyl 3-carboxypyridine-3-carboxylate (2·1 g., 23%), rhombs, m. p. 122—123°. After recrystallisation these esters had respectively m. p. 106° and 123° which are the values recorded by Kirpal.

(ii) The anhydride (3·6 g.) and methanol (2 c.c.) were heated under reflux for 10 min. and the excess of methanol removed *in vacuo*. The yields of the 3- (2·7 g., 62%) and the 2-methyl ester (0·9 g., 21%) indicate that the shorter reaction time had increased the ratio of two esters from 2 : 1 to 3 : 1. Kirpal, who used a reaction time of 4 hr., obtained the widely different ratio 1 : 10.

(iii) The anhydride (5·88 g.) and methanol (1·8 g.) were heated on the steam-bath for 2 hr. Crystallisation of the product from ethyl acetate yielded methyl 3-carboxypyridine-2-carboxylate (5·2 g., 73%), m. p. 122—123°; the filtrate slowly deposited the 3-methyl ester (1·2 g., 17%) which after crystallisation from benzene had m. p. 105—106°.

1 : 3-Dihydro-1-hydroxy-1-methoxy-3-oxofurano[3 : 4-b]*pyridine* (I).—Powdered pyridine-2 : 3-carboxylic anhydride (7·45 g.) was triturated with methanol (2 g., 1 : 2-mol.); within 5 min. a clear viscous liquid (I) resulted with rise of temperature to 48°.

Structural experiments. (i) Freshly prepared hemiacetal (I), shaken with 10 vols. of cold water, gave a clear solution which rapidly deposited pyridine-2 : 3-dicarboxylic acid quantitatively. (ii) Freshly prepared hemiacetal (I) was kept for 5—20 min. before being shaken with water: the resulting clear solution, on evaporation at low temperature, yielded methyl 2-carboxypyridine-3-carboxylate, m. p. 102—103°, almost quantitatively. (iii) After 20—30 min. the hemiacetal (I) began to solidify; the pressed solid, m. p. 100—125°, was separated by crystallisation from ethyl acetate into methyl 3-carboxypyridine-2-carboxylate, m. p. 122—123°, and methyl 2-carboxypyridine-3-carboxylate, m. p. 102—103°. (iv) After 30 min. at 60° the hemiacetal (I) was triturated with light petroleum: the product had m. p. 122—123°, showing that conversion into methyl 3-carboxypyridine-2-carboxylate was complete.

The Hydrate, 1 : 3-Dihydro-1 : 3 : 3-trihydroxy-1-methoxyfurano[3 : 4-b]*pyridine.*—Attempts to crystallise the hemiacetal (I) were unsuccessful, yet when a few drops of water were added to its concentrated ethereal solution crystals, m. p. 84°, of its hydrate separated. (ii) A few drops of water were added to freshly prepared heniacetal (I), from pyridine-2 : 3-carboxylic anhydride (7·45 g.) and methanol (2 c.c.), and the resultant clear liquid stirred: it set to a semisolid mass; this was washed with water (2 c.c.); the filtrate deposited a trace of pyridine-2 : 3-dicarboxylic acid. This washed solid, after rapid drying, weighed 6·2 g. and had m. p. 78—80° (incomplete). After 36 hr. it melted indefinitely at 84—102°. (iii) A portion (0·5 g.) of this freshly prepared material dissolved almost completely in cold ether and the solution deposited glassy rhombs (0·41 g.), m. p. 84°. (iv) Another portion (1 g.) was dissolved in water (6 c.c.) at 40° and the solution allowed to evaporate; there separated plates, m. p. 100—102° (0·9 g.), of methyl 2-carboxypyridine-3-carboxylate. The crystallised material (iii) behaves similarly. (v) Another portion (1 g.) in ethyl acetate (3 c.c.) was heated for an hour; the

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cooled solution deposited methyl 3-carboxypyridine-2-carboxylate, rhombs, m. p. 118—120° (0·78 g.); the filtrate yielded the 3-methyl ester, plates, m. p. 100—101° (0·14 g.). (vi) Another portion, after an hour, was separated by extraction with cold ether into (*a*) an insoluble part (about 20%) of m. p. 102°, alone and when mixed with methyl 2-carboxypyridine-3-carboxylate, and (*b*) a soluble part (about 80%) which separated from the solution in glassy rhombs, m. p. 84° to a clear liquid which solidified on cooling and then had m. p. 102—104° alone and when mixed with methyl 2-carboxypyridine-3-carboxylate.

The hydrate, m. p. 84° (Found: C, 48·5; H, 4·7; N, 6·7. $C_8H_9O_5N$ requires C, 48·2; H, 4·5; N, 7·0%) (0·2909 g.), was titrated with 0·107N-sodium hydroxide with phenolphthalein as indicator; each addition of alkali gave a pink colour which disappeared after a few moments (total 13·8 c.c., whence $M = 197$. $C_8H_9O_5N$ requires M, 199).

The monohydrate (0·5 g.) and methyl 2-carboxypyridine-3-carboxylate (0·5 g.) were separately heated for an hour with butan-2-ol (1 c.c.), and the resulting solutions warmed under reduced pressure to remove the butanol. In each case the product was pure methyl 3-carboxypyridine-2-carboxylate, m. p. 122—123°. Ethereal solutions of freshly prepared acetal (I) and its hydrate (IV) with diazomethane (excess) gave excellent yields of dimethyl pyridine-2 : 3-dicarboxylate, m. p. 54°.

(±)-sec.-*Butyl 3-Carboxypyridine-2- and 2-Carboxypyridine-3-carboxylate.*—A mixture of pyridine-2 : 3-dicarboxylic anhydride (30 g.) and *sec.*-butyl alcohol (20 c.c.), after an hour on the steam-bath, formed a clear solution from which needles began to separate: after an additional hour the product was almost wholly crystalline. The pressure was then reduced to remove the excess of alcohol and the residue was crystallised from hot ethyl acetate. The first crop (29·4 g.) consisted of the 2-*sec.*-butyl ester, plates, m. p. 149°: the filtrate next day yielded the 3-*sec.*-butyl ester (15 g.), needles, m. p. 129°. The 2-sec.-*butyl ester*, recrystallised from ethyl acetate, formed needles, m. p. 149—150° (Found: N, 6·1%; *M*, by titration, 222. $C_{11}H_{13}O_4N$ requires N, 6·3%; *M*, 223). The 3-sec.-*butyl ester*, recrystallised from acetone, formed needles, m. p. 129—130° (Found: N, 6·2%; *M*, 222).

(+)- *and* (−)-sec.-*Butyl 3-Carboxypyridine-2-carboxylate.*—Brucine (49·5 g.) dissolved readily in a warm solution of the (±)-2-butyl ester (28 g.) in acetone (100 c.c.); the solution soon crystallised. Filtration yielded a brucine salt (m. p. 184°; 65 g.; crop A): this was heated for 2 hr. under reflux with acetone (200 c.c.), and the suspension cooled and filtered to give crop B (45·5 g.). This, in turn, was heated under reflux with acetone (100 c.c.) for an hour, cooled, and filtered, to give crop C (36·5 g.), needles, m. p. 186°. Crop C was triturated with acetone (40 c.c.), and the suspension mixed slowly with 0·5N-sulphuric acid (116 c.c.) and shaken. The resulting brucine sulphate was removed and washed with hot acetone (20 c.c.). The aqueous acetone filtrate was slowly evaporated on a current of air, (+)-*sec.*-butyl 3-carboxypyridine-2-carboxylate (10·5 g.) separating as needles, m. p. 150—151°, $[\alpha]_D$ +22·2° (*l* 1; *c* 3·361 in $CHCl_3$).

The combined filtrates containing the more soluble fraction of the brucine salt were concentrated and mixed with 0·5N-sulphuric acid (116 c.c.) and treated as described above. The liberated (−)-*sec.*-butyl 3-carboxypyridine-2-carboxylate (10·2 g.) formed needles, m. p. 150—151°, $[\alpha]_D$ −21·1° (*l* 1; *c* 3·134 in $CHCl_3$).

(+)- *and* (−)-sec.-*Butyl 2-Carboxypyridine-3-carboxylate.*—A clear solution of the (±)-3-butyl ester (21 g.) and brucine (37 g.) in warm acetone (100 c.c.) soon deposited crystals of the brucine salt. This (crop A; 46 g.) was removed, washed with acetone, and dissolved in warm chloroform (20 c.c.). Dilution with acetone (40 c.c.) yielded crop B (34 g.). Repetition of the process yielded crop C (28·7 g.) as needles, m. p. 186°. Crop C (25 g.), triturated with acetone (70 c.c.) and 0·5N-sulphuric acid (81 c.c.) and treated as described above, yielded (+)-*sec.*-butyl 2-carboxypyridine-3-carboxylate (6·8 g.) which separated from acetone in needles, m. p. 130—131°, $[\alpha]_D$ +10·9° (*l* 1; *c* 4·60 in $CHCl_3$). The more soluble fraction of the brucine salt contained in the filtrates, which it is essential to concentrate *without heating*, after decomposition as described above, yielded (−)-*sec.*-butyl 2-carboxypyridine-3-carboxylate (7·1 g.) which separated from acetone in needles, m. p. 130—131°, $[\alpha]_D$ −8·6° (*l* 1; *c* 3·86 in $CHCl_3$).

When the filtrates containing the brucine salt were concentrated on the steam-bath before decomposition, the product was the more stable (−)-*sec.*-butyl 3-carboxypyridine-2-carboxylate, m. p. 150—151°, $[\alpha]_D$ −12° in $CHCl_3$.

The brucine salt (1 g.) of *sec.*-butyl 3-carboxypyridine-2-carboxylate was heated at 190° until completely molten, cooled, and decomposed with hydrochloric acid. Crystallisation of

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the liberated product from cold acetone yielded *sec.*-butyl 2-carboxypyridine-3-carboxylate (0·15 g.), m. p. and mixed m. p. 130—131°.

Conversion of (+)-sec.-*Butyl 2-Carboxypyridine-3-carboxylate into* (+)-sec.-*Butyl 3-Carboxypyridine-2-carboxylate.*—A solution of the (+)-3-ester (1 g.) in ethyl acetate (5 c.c.) was heated under reflux for 2 hr.; after cooling, it gave the (+)-2-ester (0·5 g.) which, after recrystallisation, had m. p. 150—151°, $[\alpha]_D$ +20·8° (*l* 1; *c* 4·850 in $CHCl_3$).

The (±)-3-ester (1 g.) was converted after 1 hr. into the (±)-2-ester (0·48 g.); the unchanged (±)-3-ester (0·39 g.) isolated from the filtrate was heated under reflux for 2 hr. in ethyl acetate; this solution deposited the (±)-2-ester (0·15 g.), needles, m. p. and mixed m. p. 149—150°.

Conversion of (±)-butyl 3-carboxypyridine-2-carboxylate into (±)-*sec.*-butyl 2-carboxypyridine-3-carboxylate occurred at 155—160° in 0·5 hr.; the molten product set to a crystalline mass, m. p. and mixed m. p. 129—130°.

Decarboxylations.—(−)-*sec.*-Butyl 3-carboxypyridine-2-carboxylate, $[\alpha]_D$ −21·1° (5 g.), and a little copper powder were heated at 180—185° under reduced pressure. After an hour, when reaction ceased, the residual liquid was dissolved in ether and washed with sodium carbonate solution. The resultant (−)-*sec.*-butyl nicotinate (2·1 g.) had b. p. 86—87°/0·8 mm., n_D^{20} 1·4913, $[\alpha]_D$ −21·8° (*l* 1; *c* 3·990 in $CHCl_3$).

The corresponding (±)-ester similarly yielded (±)-sec.-*butyl nicotinate*, b. p. 86—87°/0·8 mm., n_D^{20} 1·4912 (Found: N, 7·7. $C_{10}H_{13}O_2N$ requires N, 7·3%).

(±)-*sec.*-Butyl nicotinate, prepared in excellent yield from nicotinoyl chloride, (±)-butan-2-ol and pyridine, had b. p. 92°/2 mm., n_D^{20} 1·4913 (Found: N, 7·8%). When the (±)butanol was replaced by (+)-butan-2-ol, α_D^{20} +4·17° (*l* 0·5), the resulting (−)-*sec.*-butyl nicotinate, n_D^{20} 1·4914, had $[\alpha]_D^{20}$ −16·9 (*l* 1; *c* 4·98 in $CHCl_3$). Since the (+)-butan-2-ol had only 74·7% of its maximum rotation, optically pure (−)-*sec.*-butyl nicotinate will probably show $[\alpha]_D^{20}$ −22·6°. (+)-Butan-2-ol, α_D +3·01° (*l* 0·5), gave butyl nicotinate, $[\alpha]_D$ −12·1°, which suggests that the rotation of optically pure *sec.*-butyl nicotinate will be $[\alpha]_D^{20}$ −21·8°.

(+)-*sec.*-Butyl 2-carboxypyridine-3-carboxylate and a little copper powder at 160—165° gave butyl nicotinate, n_D^{20} 1·4912, $[\alpha]_D$ +21·9° (*l* 1; *c* 4·64 in $CHCl_3$). The (±)-3-ester yielded (±)-*sec.*-butyl nicotinate, n_D^{20} 1·4913.

Ethyl Hydrogen Metahemipinate.—A solution of metahemipinic anhydride (0·5 g.) in absolute ethanol (2 c.c.) was evaporated at room temperature after 4 hr.; the residue was unchanged anhydride. Presence of acetone did not alter the result. The anhydride (0·5 g.), when heated in absolute ethanol (3 c.c.) under reflux for 2 hr., gave unchanged anhydride but after 4 hr. yielded ethyl hydrogen metahemipinate (0·4 g.), m. p. 125—127°: after one recrystallisation, this had m. p. 129° (Rossin [7] gives m. p. 127°). Addition of pyridine brings about the reaction within 2 hr.

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BATTERSEA POLYTECHNIC, LONDON, S.W.11. [*Received, January 28th*, 1957.]

[7] Rossin, *Monatsh.*, 1891, **12**, 489.

493. *The Alkaloids of the Amaryllidaceae. Part II.* Hæmanthine and a New Alkaloid Distichine from* Boöphone disticha *Herb.*

By Angela N. Bates, J. K. Cooke, L. J. Dry, A. Goosen, H. Krüsi, and F. L. Warren.

The extract of *Boöphone disticha* Herb. contains lycorine, hæmanthine (now obtained crystalline), and a small quantity of another alkaloid isolated as its picrate, $C_{21}H_{22}O_{11}N_4$, whilst the principal constituent is a new alkaloid (distichine) $C_{19}H_{21}O_5N$. Derivatives and ultraviolet and infrared spectra of hæmanthine and distichine are recorded.

The extract of the bulbs of *Boöphone disticha* Herb. (*B. toxicaria, Buphane disticha*) has been used as an arrow poison by the bushmen and Hottentots whilst the Xosas employed it to combat " red water " in cattle.[1] Juritz [2] showed that the bulbs contained alkaloids, but the first thorough analysis of the different constituents was made by Tutin [3] in 1911, who isolated lycorine and an alkaloid buphaninine, and indicated the presence of three minor alkaloids. Lewin [4] reported another alkaloid, hæmanthine, $C_{18}H_{23}O_7N$, which he characterised as the hydrochloride, nitrate, and chloroplatinate, though Tutin [5] maintained that it was a mixture. Cooke and Warren [6] recently isolated Lewin's liquid hæmanthine again from *B. disticha* and corrected the formula to $C_{18}H_{21}O_5N$; finally Goosen and Warren [7] identified it with buphanitine.

The bulbs of *B. disticha* have been collected from different parts of Southern Africa and at different seasons during ten years. On no occasion have we isolated an alkaloid corresponding to $C_{17}H_{19}O_4N$, m. p. 189°, which Humbold and Taylor [8] recently reported from this plant. Following Tutin's procedure [3] we confirmed the isolation of the non-alkaloidal material, but copper was never detected in the extract. The alkaloid fraction has now been separated to give lycorine, hæmanthine, a new alkaloid distichine, and a water-soluble alkaloid, isolated as the picrate, $C_{21}H_{22}O_{11}N_4$. The extraction procedure recorded in this paper, devised for the ready extraction of distichine and hæmanthine, was based on the facts that hæmanthine is much less soluble in ether, more readily adsorbed on alumina, and more basic than distichine, and that distichine hydrochloride is soluble in chloroform.

Distichine is the main alkaloid in *B. disticha* collected in the environs of Pietermaritzburg, Pretoria, Bloemfontein, and Grahamstown. It crystallised from aqueous methanol as a hydrate, $C_{19}H_{21}O_5N,0{\cdot}75H_2O$, from which the anhydrous alkaloid was obtained by distillation under reduced pressure. It is extremely stable to heat and some unchanged alkaloid was recovered from zinc dust distillation of the alkaloid. It gave a crystalline platinichloride, perchlorate, picrate, and styphnate, whose analyses corresponded to the above formula when the salts were prepared directly from the pure alkaloid but only after numerous crystallisations if made from the non-crystalline base (the melting points were no criterion of purity). The molecular weight was measured by comparison

* Part I, *J. S. African Chem. Inst.*, 1953, **6**, 2.

[1] Watt and Breyer-Brandwyk, " The Medicinal and Poisonous Plants of Southern Africa," Livingstone, Edinburgh, 1932, p. 25; Steyn, " The Toxicology of Plants in South Africa," Central News Agency, S. Af., 1934, p. 539.
[2] Juritz, *Rep. Senior Analyst for* 1903, *Cape of Good Hope*, 1904, **59**, 63; *Rep. S. African Assoc. Adv. Sci.*, 1911, **8**, 98.
[3] Tutin, *J.*, 1911, **99**, 1240.
[4] Lewin, *Arch. Exp. Path. Pharm.*, 1912, **68**, 333; 1912, **70**, 302.
[5] Tutin, *ibid.*, 1912, **69**, 314.
[6] Cooke and Warren, *J. S. African Chem. Inst.*, 1953, **6**, 2.
[7] Goosen and Warren, *Chem. and Ind.*, 1957, 267.
[8] Humbold and Taylor, *Canad. J. Chem.*, 1955, **33**, 1268.

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of the ultraviolet extinction coefficient [9] of the picrates of distichine and lycorine. Formation of a methiodide and a methoreineckate established presence of a tertiary nitrogen atom. Zeisel determination showed two methoxy-groups, and Berzoa's test [10] indicated a methylenedioxy-group.

Hæmanthine, $C_{18}H_{21}O_5N$, has now been obtained as hemihydrated needles, m. p. 230°, and as rhombohedra, m. p. 240°, which lost solvent of crystallisation at 130° to give a sublimate, m. p. 228°. Its hydrochloride likewise was obtained as a sesquihydrate, monohydrate, and semihydrate. It gave a crystalline nitrate, perchlorate, and picrate, also a methiodide and methoreineckate so that the nitrogen atom is tertiary, and it contains a methoxyl and a methylenedioxy-group.[10] Zerewitinov's reaction disclosed two active hydrogen atoms and hæmanthine readily formed an amorphous diacetate, and once a crystalline monoacetate.

Infrared bands at 9·0, 9·67, and 10·57 μ for distichine and at 9·71 and 10·72 μ for hæmanthine indicate a methylenedioxyphenyl group in both alkaloids. Bands at 2·82 and 2·87 μ for hæmanthine are attributed to the hydroxyl groups. Strong absorption at 6·18 and 6·16 μ for distichine and hæmanthine respectively is in contrast with the weak absorption in this region for lycorine, and, by analogy with observations by Wildman and his co-workers,[11] may be attributed to the methoxy-group in the benzene nucleus. The ultraviolet spectrum of distichine [$\lambda_{min.}$ 260 mμ (log ε 2·49); $\lambda_{max.}$ 285 mμ (log ε 3·15)] is almost identical with that of hæmanthine ($\lambda_{min.}$ 260; $\lambda_{max.}$ 285 mμ; log ε 2·66 and 3·23 respectively). The similarity with hydrocotarnine ($\lambda_{max.}$ 287 mμ, log ε 3·23) supports the assignment of the methoxy-group to the benzene nucleus.

Experimental

Microanalyses are by Y. Merchant, ultraviolet and infrared measurements by Dr. E. C. Leisegang and M. E. von Klemperer.

Extraction.—Seventy bulbs of *Boöphone disticha* Herb., collected in late May on the outskirts of Pietermaritzburg, were sliced and dropped into boiling ethanol, then dried, crushed (7 kg.), and extracted with ethanol (Soxhlet). The extract together with the first ethanol solution was flash-evaporated under reduced pressure and the concentrate (4 l.) steam-distilled for 2 hr. The cooled solution was filtered, washed with ether (2 × 1 l.), basified with sodium carbonate, and extracted with chloroform (6 × 1 l.). The extract gave a dark brown gum (200 g.) which was ground to a powder with plaster of Paris and extracted with boiling ether (E) (5 × 1 l.) and then with chloroform (F_1) (4 × 1 l.).

The ether extract (E) gave a gum (120 g.) which was treated with N-hydrochloric acid (300 ml.), filtered, and extracted with ether (4 × 100 ml.), which removed acetovanillone, and with chloroform (F_2) (6 × 200 ml.). The acid solution was made alkaline with sodium carbonate, to give a voluminous precipitate, and extracted with ether (E_2) (4 × 250 ml.) and chloroform (F_3) (3 × 200 ml.). The hydrochloride from (F_2) gave a base soluble in ether (E_1).

The ether solutions E_1 and E_2 gave gums which were lixiviated with ether, and this ether solution was extracted stepwise with 2N-hydrochloric acid (4 × 2·5 ml.; 50 ml.; 4 × 2·5 ml.). Each fraction was basified and extracted with chloroform. Fractions 1—3 gave crystals (H) on the addition of ether; fractions 4—7 were ether-soluble gums which slowly crystallised (D).

The combined chloroform extracts (F_1 and F_3) gave a gum (60 g.) which in a little chloroform was percolated through alumina (360 g.; grade II). The column was washed with ether; the first runnings (200 ml.) gave coloured amorphous alkaloidal material, and the later fraction (1·2 l.) on concentration gave only a small quantity of crystals (H), m. p. *ca.* 226°. The column was fractionally eluted with (i) chloroform–ether (1 : 1; 3 × 400 ml.), (ii) chloroform (3 × 400 ml.), and (iii) methanol (2 l.). Fraction (i) gave gums which were dissolved in chloroform and fractionally precipitated with ether, to give first resin and later crystals (H), m. p. *ca.* 226°. Fraction (ii) behaved similarly. The resin and that from fraction (iii) were

[9] Cunningham, Dawson, and Spring, *J.*, 1951, 2305.
[10] Berzoa, *Analyt. Chem.*, 1954, **26**, 1971.
[11] Wildman and Kaufman, *J. Amer. Chem. Soc.*, 1955, **77**, 4807; cf. Brigs, Highet, Highet, and Wildman, *ibid.*, 1956, **78**, 2899.

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re-chromatographed, to give a further quantity of crystals (H) (3·7 g.), m. p. *ca.* 226°, and a little lycorine, m. p. 260°.

Distichine.—The crystals (D) recrystallised from methanol–water as needles of *distichine*, m. p. 144°, $[\alpha]_D^{20}$ −39° (*c* 1 in $CHCl_3$) (Found: C, 64·2, 63·7; H, 6·8, 6·8; OMe, 19·5. $C_{19}H_{21}O_5N,0{\cdot}75H_2O$ requires C, 64·0; H, 6·35; 2OMe, 17·4%). Distichine distilled at 140°/0·3 mm. to an oil, which solidified (m. p. 90—92°) (Found: C, 66·7, 66·8; H, 6·2, 6·4. $C_{19}H_{21}O_5N$ requires C, 66·5; H, 6·2%). The *platinichloride* crystallised from water as orange-yellow rods, m. p. 223° (Found: C, 40·7, 40·8; H, 4·4, 4·2; Pt, 18·7, 18·7. $C_{38}H_{44}O_{10}N_2PtCl_6,H_2O$ requires C, 40·9; H, 4·2; Pt, 17·5%). The *perchlorate*, obtained by the addition of sodium perchlorate to distichine hydrochloride, crystallised from water in rhombohedra, m. p. 247° (Found: C, 51·8; H, 4·9. $C_{19}H_{22}O_9NCl$ requires C, 51·4; H, 5·0%). The *picrate* crystallised from alcohol in yellow needles, m. p. 235° (Found: C, 52·9, 52·7, 52·2, 52·6; H, 4·45, 3·95, 4·1, 4·6; N, 10·1; OMe, 10·4%; *M*, 563. $C_{25}H_{24}O_{12}N_4$ requires C, 52·5; H, 4·2; N, 9·8; 2OMe, 10·8%; *M*, 572). The *styphnate* crystallised from ethanol as yellow rectangular laminæ, m. p. 239—241° (Found: C, 50·5, 50·6; H, 4·1, 3·7. $C_{25}H_{24}O_{13}N_4$ requires C, 51·0; H, 4·1%).

Distichine methiodide crystallised from hot methanol as long colourless needles, m. p. 271°, $[\alpha]_D^{24}$ +7·7° (*c* 0·9 in EtOH) (Found: C, 49·7, 49·8, 49·6; H, 5·2, 5·4, 5·5; N, 2·5. $C_{20}H_{24}O_5NI$ requires C, 49·5; H, 5·0; N, 2·9%). The *methoreineckate* was obtained as an amorphous pink solid by the addition of water to an acetone solution (Found: C, 41·2; H, 5·0. $C_{24}H_{32}O_5N_7S_4Cr,2H_2O$ requires C, 41·3; H, 5·0%).

Hæmanthine.—The combined crystals (H) (13 g.) in chloroform were treated with ether until the solution was slightly turbid; hæmanthine separated as needles, m. p. 224°, raised only after several recrystallisations to 230°, $[\alpha]_D^{20}$ −101·6° (*c* 1 in EtOH) (Found: C, 63·8; H, 6·7; N, 4·5; OMe, 8·9. $C_{18}H_{21}O_5N,0{\cdot}5H_2O$ requires C, 63·6; H, 6·5; N, 4·1; OMe, 9·1%). The crystals sublimed at 180°/0·1 mm. as needles, m. p. 197—199° (Found: C, 65·4; H, 6·8. $C_{18}H_{21}O_5N$ requires C, 65·2; H, 6·4%). Hæmanthine crystallised from ethanol in rhombohedra which lost solvent of crystallisation at 130° and then had m. p. 240° with sublimation (Found: C, 63·8; H, 6·7%). The sublimate had m. p. 228°.

Hæmanthine Hydrochloride.—Hæmanthine in dilute hydrochloric acid was evaporated at 100° and the product crystallised twice from water gave *hæmanthine hydrochloride* as colourless needles, m. p. 180° (Found: C, 54·4; H, 6·4; N, 3·8. $C_{18}H_{22}O_5NCl,1{\cdot}5H_2O$ requires C, 54·7; H, 6·4; N, 3·5. Found, after drying at 100°/0·1 mm.: C, 56·1; H, 6·5; N, 3·2. $C_{18}H_{22}O_5NCl,H_2O$ requires C, 56·0; H, 6·3; N, 3·6%). Hæmanthine in ethanol was treated with 1 mol. of concentrated hydrochloric acid, and ether was added until the solution was turbid. The crystals were recrystallised in the same manner, to give *hæmanthine hydrochloride* as needles, m. p. 265°, $[\alpha]_D$ +13° (*c* 1 in H_2O) (Found: C, 57·4; H, 6·4; Cl, 10·0. $C_{18}H_{22}O_5NCl,0{\cdot}5H_2O$ requires C, 57·4; H, 6·2; Cl, 9·7%). The *platinichloride* separated from hot water as light orange crystals, m. p. 204° (Found: C, 39·6; H, 4·5; Pt, 19·8. $C_{36}H_{48}O_{12}N_2Cl_6Pt$ requires C, 39·0; H, 4·4; Pt, 17·6%). The *nitrate* crystallised from alcohol and moist ether as needles, m. p. 129° (Found: C, 52·2; H, 6·2. $C_{18}H_{22}O_8N_2,H_2O$ requires C, 52·4; H, 5·9%). The *perchlorate* formed as above crystallised from water in flat needles, m. p. 99—100° (Found: C, 46·8; H, 5·8. $C_{18}H_{22}O_9NCl,1{\cdot}5H_2O$ requires C, 47·1; H, 5·5%). The *picrate*, purified by the addition of water to its alcoholic solution, and finally by cooling a hot aqueous solution, was obtained as a yellow powder (Found: C, 51·2; H, 4·4. $C_{24}H_{24}O_{12}N_4$ requires C, 51·4; H, 4·3%). The *methiodide*, prepared in hot methanol, crystallised therefrom as needles, m. p. 248°, $[\alpha]_D^{18}$ −70·3° (*c* 1 in H_2O) (Found: C, 46·7; H, 5·8; N, 2·4. $C_{19}H_{24}O_5NI,H_2O$ requires C, 46·4; H, 5·3; N, 2·8%). The *methoreineckate* was precipitated as a pink amorphous powder (Found: C, 40·1; H, 5·1. $C_{23}H_{32}O_6N_7S_4Cr$ requires C, 40·5; H, 4·7%).

Mono- and Di-acetylhæmanthine.—Hæmanthine (0·5 g.), acetic anhydride (10 ml.), benzene (20 ml.), and acetyl chloride (4 ml.) were refluxed for 1 hr. The product in chloroform was chromatographed over alumina, and the concentrated benzene eluate treated with light petroleum until turbid. *Monoacetylhæmanthine* crystallised in needles, m. p. 199° (*c* 1 in $CHCl_3$) (Found: C, 64·6; H, 6·2; Ac, 10·6. $C_{20}H_{23}O_6N$ requires C, 64·3; H, 6·2; Ac, 11·3%). On all other occasions *diacetylhæmanthine* separated as an amorphous white solid (Found: C, 62·2; H, 6·2; Ac, 21·3. $C_{22}H_{25}O_7N,0{\cdot}5H_2O$ requires C, 62·3; H, 6·2; Ac, 19·8%).

Alkaloid Picrate, m. p. 129—131°.—The bulbs were extracted by Tutin's method.[3] The pentyl alcohol extract was poured into ether, filtered, and washed with water. The aqueous

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solution was filtered from a little lycorine, and treated with picric acid, and the product recrystallised from hot water to give a *picrate*, m. p. 129—131° (Found: C, 49·8; H, 4·4. $C_{21}H_{22}O_{11}N_4$ requires C, 49·8; H, 4·4%).

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494. *Boiling Points of Homologous Liquids.*

By G. R. SOMAYAJULU and SANTI R. PALIT.

The equation $T_b = a\sqrt{(\Sigma Z)} + b$ has been found to represent the boiling points of many homologous series, *e.g.*, *n*-alkyl fluorides, chlorides, bromides, iodides, acids, amines, aldehydes, ketones, *n*-alkyl-benzenes, *-cyclo*hexanes, and *-cyclo*hex-1-enes, where ΣZ is the atomic number sum and a and b are constants characteristic of any particular series. For *n*-alkanes, *n*-alkenes, and *n*-alkynes the above equation is not applicable, but T_b is found to be related linearly to the cube root of ΣZ; for alcohols, thiols, esters, and ethers T_b is related approximately linearly to ΣZ.

THE boiling points of a series of compounds, especially halides of similar structure and having an equal number of atoms in the molecule, have been successfully correlated with the atomic number of the varying atoms in the series.[1] We now attempt to correlate the boiling points of a homologous series by using atomic number as the independent parameter. We now suggest the empirical relation (1) between the boiling point, T_b, in any homologous series and the sum of the atomic numbers of the atoms in the molecule (ΣZ), a and b being constants.

$$T_b = a\sqrt{(\Sigma Z)} + b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Aldehydes, Ketones, Acids, Primary, Secondary, and Tertiary Amines and Halides.—We illustrate equation (1) with eight homologous *n*-alkyl series in Fig. 1 (bromides and iodides not shown). The plot of T_b against the square-root of ΣZ gives straight lines agreeing with the equation, except for occasional slight departure for the first member of a series.

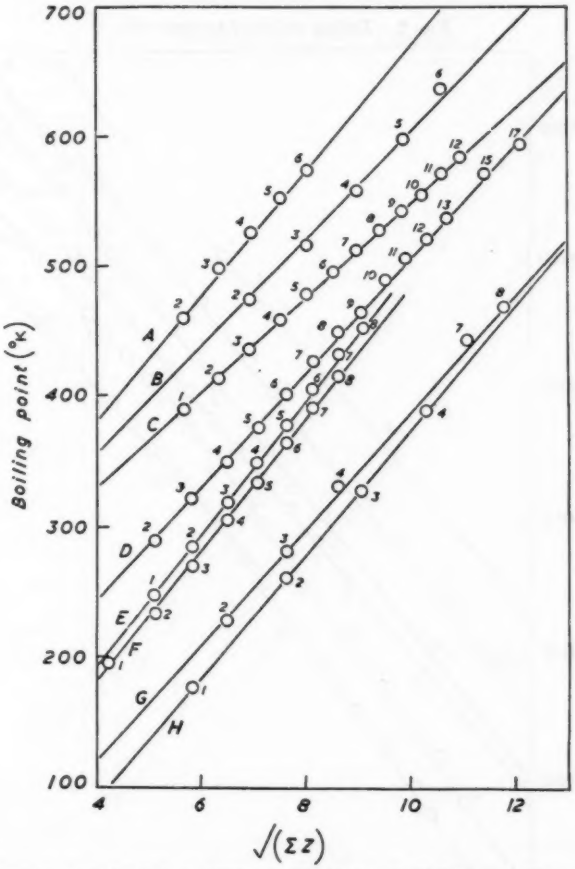
The least-square values of a and b are compiled in the Table (1—13). The slopes for all the series are of the same order of magnitude, those for the halides being the highest and that for the fatty acids the lowest. It is remarkable that the value of a lies within such a narrow range for these various types of compounds. With regard to the value of b, the boiling point corresponding to zero atomic number, the highly electronegative elements, *viz.*, the halides, lead to the lowest values and the carboxylic acids the highest; the value of b decreases continuously from primary through secondary to tertiary amine. Since the variation in slope among the different homologous series is small, it is clear that the intercept (b) plays the more important part in determining boiling point.

	Homologous Series	a	b	p		Homologous Series	a	b	p
1.	*n*-Alkyl fluorides	51·31	− 26·70	½	11.	*n*-Alkyl-benzenes	46·88	52·57	½
2.	,, chlorides	52·06	− 17·05	,,	12.	,, *-cyclo*hexanes ...	49·54	9·16	,,
3.	,, bromides	57·54	−102·5	,,	13.	,, *-cyclo*hex-1-enes	47·24	34·10	,,
4.	,, iodides	61·10	−164·0	,,	14.	*n*-Alkanes	154·40	−223·90	½
5.	,, aldehydes	48·87	36·85	,,	15.	*n*-Alk-1-enes	154·45	−222·10	,,
6.	,, ketones	44·11	67·20	,,	16.	*n*-Alk-1-ynes	144·44	−168·78	,,
7.	,, acids	36·17	188·0	,,	17.	Normal alcohols	2·44	288·0	1
8.	,, primary amines...	45·43	55·56	,,	18.	*n*-Alkyl ethers	3·58	157·10	,,
9.	,, secondary amines	46·52	28·10	,,	19.	,, acetates	2·76	220·80	,,
10.	,, tertiary amines ...	47·95	− 5·05	,,	20.	*n*-Alkanethiols	3·87	178·0	,,

[1] Somayajulu, *Indian J. Phys.*, 1956, **30**, 258.

Hydrocarbons.—For simple hydrocarbons, *viz.*, alkanes, alkenes, and alkynes, the simple square-root plot apparently gives two straight lines intersecting near C_{10} in all cases (Fig. 2). We do not, however, attach any special importance to this, as good straight lines

FIG. 1. *Boiling points of* n-*alkyl derivatives.*



A, R·CHO (T_b + 150°); *B*, R_2CO (T_b + 100°); *C*, R·CO_2H; *D*, R·NH_2; *E*, RCl; *F*, RF; *G*, R_2NH (T_b − 100°); *H*, R_3N (T_b − 100°).
In all Figures the numerals against each point represent the number of carbon atoms in the alkyl group.

are obtained by changing the exponent to 1/3 as is shown in Fig. 3. It appears that the general relation is of the form,

$$T_b = a(\Sigma Z)^p + b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

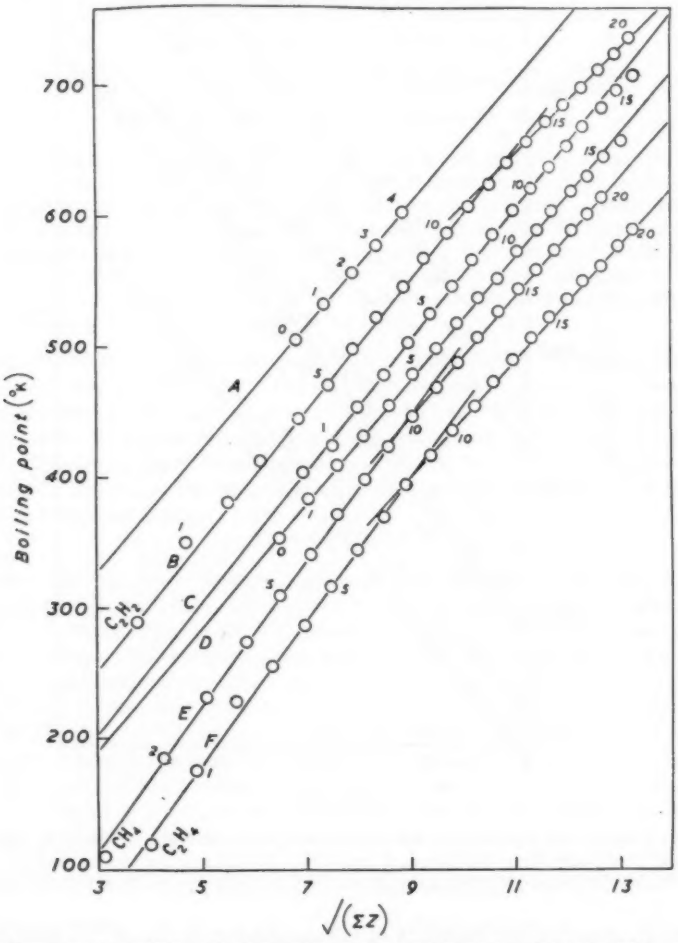
where p is usually 1/2 but differs from this value for simple aliphatic hydrocarbons and a few other series. However, for other hydrocarbon series, *viz.*, alkyl-benzenes, *-cyclo*-hexanes, and *-cyclo*hexenes, the square-root relation is quite good (Fig. 2), though a slight change of exponent makes it even better. The values of the constants a and b and of the exponent p are also collected in the Table.

Comparison with Previous Equations.—Several equations have already been suggested

to correlate the boiling point with either the molecular weight or the number of carbon atoms as the variable parameter; our suggestion of atomic number is novel. A summary of these equations has been given by Partington [2] and the situation has been lately discussed by Varshni.[3] The most successful is that of Boggio-Lera [4]

$$T_b^2 = AM + b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

FIG. 2. *Boiling points of hydrocarbons.*



A, Alkyl*cyclo*hexenes ($T_b + 150°$); *B*, alkynes (treated as alkylacetylenes) ($T_b + 100°$); *C*, alkyl*cyclo*hexanes; *D*, alkylbenzenes; *E*, alkanes (treated as alkylmethanes); *F*, alkenes (treated as alkylethylenes) ($T_b - 50°$).

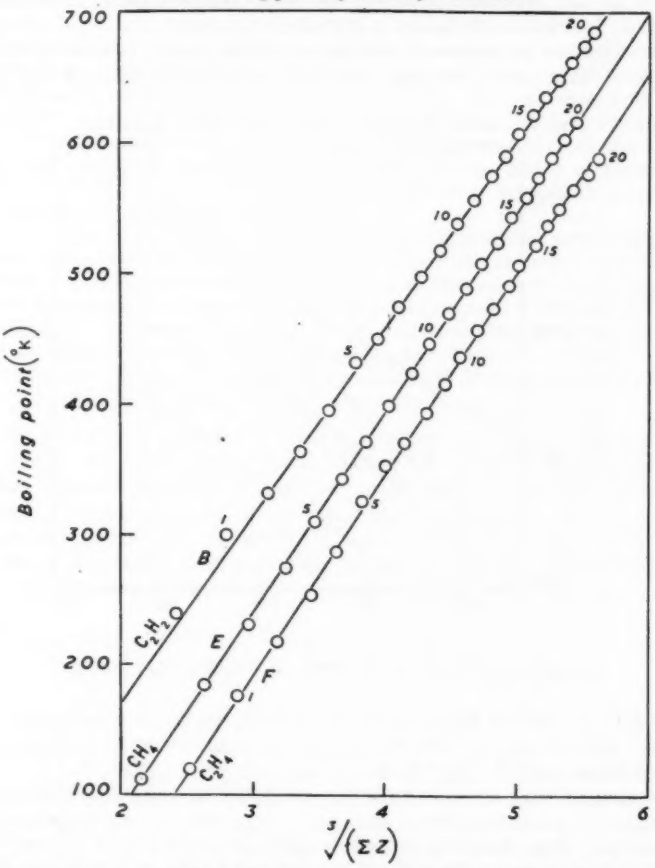
where M is the molecular weight. This equation evidently is in essence similar to ours and gives good correlation in many cases. We have compared Boggio-Lera's equation

[2] Cf. Partington, "An Advanced Treatise on Physical Chemistry," Vol. II, Longmans, Green and Co., London, 1951, pp. 275—303.
[3] Varshni, *J. Indian Chem. Soc.*, 1953, **30**, 169; 1955, **32**, 211.
[4] Boggio-Lera, *Gazzetta*, 1899, **29**, 441.

with ours and have found that in the twenty series studied by us Boggio-Lera's equation is as good as ours in 7 cases, inferior in 3 cases (series 11, 12, and 13 of the Table), and wrong in 10 cases (series 8—10 and 14—20). We do not, therefore, favour an equation of the form of Boggio-Lera's even with atomic number as the variable parameter (*i.e.*, T_b^2 linear in, say, ΣZ).

Other equations which have attracted attention are by Nekrassov,[5] who has attempted

FIG. 3. *Boiling points of linear hydrocarbons.*



B, Alkynes (treated as alkylacetylenes) ($T_b + 50°$); *E*, alkanes (treated as alkylmethanes); *F*, alkenes (treated as alkylethylenes) ($T_b + 50°$).

to correlate T_b with some structural constants (a simple graphical plot shows its weakness) and by Van Arkel,[6] which correlates T_b with the molar volume of halides. Somayajulu [1] has shown that for halides atomic number effectively correlates the boiling points and no molar-volume data are necessary. The boiling point for halides from this standpoint will be dealt with in greater detail in a later communication.

Alcohols, Thiols, Ethers, and Esters.—So far we have dealt with practically all mono-substituted alkanes except the above four series, which do not obey the square-root

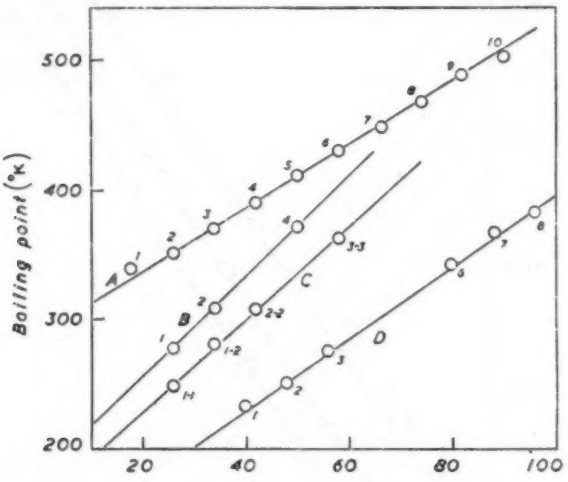
[5] Nekrassov, *Z. phys. Chem.*, 1929, *A*, **141**, 378; 1930, *A*, **148**, 216.
[6] Van Arkel, *Rec. Trav. chim.*, 1932, **51**, 1081; 1933, **52**, 719, 733; 1934, **53**, 91, 146.

relation but an equation of the form of eqn. 2 with $p = 1$ (Fig. 4). This relation is rather approximate and is essentially the same as is already known that in such series T_b is more or less linear with M. It is surprising that these simple compounds should behave so differently from the rest. The values of the constants a and b for these four series have been also collected in the Table.

Boiling Point and Other Properties.—Since we have correlated T_b with ΣZ and since the latter has been correlated [1, 7] with many physical properties, it follows that T_b will be simply related to such properties. One of the most evident is molar refraction, R, which is well known to be linear with ΣZ for a homologous series.

Some other physical properties depending on boiling point can also be correlated with atomic number. Thus from Trouton's rule, and also from Guldberg's rule, the heat of

FIG. 4. *Boiling points of alcohols, thiols, ethers, and esters.*



A, R·OH; *B*, R·SH; *C*, R′·O·R″; *D*, $CH_3 \cdot CO_2R$ ($T_b - 100$).

vaporisation and the critical temperature should both be linear with $\sqrt{(\Sigma Z)}$ in a homologous series. Also, from the semi-theoretical equation recently developed by Palit [8] that $\log \eta M$ is linear with T_b, $\log \eta M$ should be linear with $\sqrt{(\Sigma Z)}$.

From our present work it seems that the possibility of expressing boiling point as an additive function of properties of the atoms or groups present in a molecule seems to be rather remote, and that the atomic-number sum ΣZ (equal to the number of electrons in a molecule) is a fundamental property of an organic molecule and many of its physical properties are a function of it.

All data on boiling point have been collected from standard sources.[9-11] We thank C.S.I.R., Government of India, for financial assistance (to G. R. S.).

INDIAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,
CALCUTTA 32, INDIA.

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[7] Somayajulu and Palit, *Indian J. Phys.*, 1956, **30**, 262.
[8] Palit, *J.*, 1956, 2740.
[9] "Selected values of physical and thermodynamic properties of hydrocarbons and related compounds," American Petroleum Institute Research Project, Carnegie Press, Pittsburgh, 1953.
[10] Rodd, "Chemistry of Carbon Compounds," Vol. I, Elsevier, New York, 1953.
[11] Hodgman, "Handbook of Physics and Chemistry," Chemical Rubber Publ. Co., Ohio, 1948.

XUM

495. *Magnetic Studies with Copper(II) Salts. Part II.*[1] *Anomalous Paramagnetism and δ-Bonding in Anhydrous and Hydrated Copper(II) n-Alkanoates.*

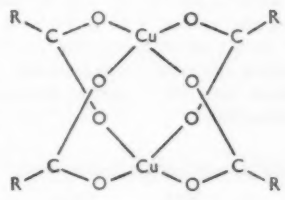
By R. L. Martin and Hanneke Waterman.

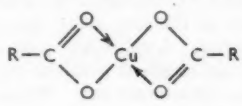
The temperature variation of the magnetic susceptibility, between 90° and 400° K, is reported for copper(II) propionate, butyrate, laurate (C_{12}), stearate (C_{18}), and behenate (C_{22}). The variation is anomalous in that antiferromagnetic rather than Curie-law characteristics are observed. For all the compounds, whether hydrated or anhydrous, the susceptibility at first increases with rising temperature, passes through a maximum in the range 278° ± 28° K, and then decreases. This behaviour so closely resembles that of copper acetate (cf. Part I [1]) that it is concluded that all the salts have fundamentally identical molecular structures, consisting of binuclear inner complexes $[Cu_2(R{\cdot}CO_2)_4(H_2O)_{0\text{ or }2}]$ involving a very weak covalent δ bond between the copper atoms.

The anomalous magnetic behaviour can be interpreted by assuming that within each binuclear molecule the two copper atoms interact strongly through exchange forces, forming a lower singlet (diamagnetic) and an upper triplet (paramagnetic) state. The experimental results for all five compounds closely fit an expression containing J, the singlet–triplet separation, which also measures twice the exchange energy associated with the copper–copper δ bond. For the present compounds, values of J lie in the narrow range 309 ± 31 cm.$^{-1}$, *i.e.*, approximately 1 kcal. mole^{-1}.

In Part I [1] the anomalous magnetic behaviour of copper(II) acetate was discussed in the light of a recent crystal-structure determination by Niekerk and Schoening.[2] The unusually low magnetic moment was shown to arise from exchange demagnetisation between copper atoms in each binuclear $[Cu_2(CH_3{\cdot}CO_2)_4(H_2O)_2]$ molecule, the exchange resulting from an unusual type of overlap of atomic orbitals, namely, lateral overlap of two $3d_{x^2-y^2}$ orbitals so oriented that their lobar planes are parallel. Such overlap produces a covalent δ bond between copper atoms, copper acetate being the first compound in

(I)





(II)

R = *n*-alkyl

which this type of bond has been suggested as the sole covalent bond between two atoms.

It seemed probable that further examples of the binuclear configuration and δ-bonding would be found among the higher homologues of copper(II) alkanoates, since the dimensions of the potential bridging carboxylate group are not likely to depend significantly on the length of the attached alkyl chain. Furthermore, construction of Catalin molecular models clearly demonstrated that the *n*-alkyl chains can be easily accommodated around the periphery of the molecule without sterically hindering formation of the binuclear $[Cu_2(R{\cdot}CO_2)_4]$ molecule illustrated in structure (I).

Magnetic measurements, over a range of temperature, provide a particularly sensitive and convenient method for testing this hypothesis. If the salts adopt the proposed binuclear configuration their magnetic moments will fall to approximately the value

[1] Part I, Figgis and Martin, *J.*, 1956, 3837.
[2] Niekerk and Schoening, *Acta Cryst.*, 1953, **6**, 227.

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observed for copper acetate. Further, the susceptibility–temperature curves will exhibit antiferromagnetic rather than Curie-law characteristics, closely matching the curve of the acetate. Accordingly, the magnetic susceptibilities of the copper(II) salts of propionic, butyric, lauric, stearic, and behenic acids have been measured between 90° and 400° K. The propionate and butyrate were examined both in anhydrous and hydrated forms, to established whether dehydration modifies the structure. The three higher homologues are anhydrous.

Experimental

Materials.—Copper(II) propionate and butyrate were prepared from excess of the diluted acid and E. Merck's " purissimus " grade copper carbonate. After effervescence had ceased the solutions were filtered and allowed to crystallize. Recrystallisation of the propionate from hot dilute propionic acid yielded dark green crystals of the monohydrate (Found : C, 31·6; H, 5·3; Cu, 27·7. Calc. for $CuC_6H_{10}O_4,H_2O$: C, 31·6; H, 5·3; Cu, 27·9%). Recrystallisation of the butyrate from 1 : 1 butyric acid–water yielded green crystals of the monohydrate (Found : C, 37·8; H, 6·2; Cu, 24·8. Calc. for $CuC_8H_{14}O_4,H_2O$: C, 37·6; H, 6·3; Cu, 24·8%). The anhydrous propionate and butyrate were prepared from the hydrated salts by dehydration at 100° c over phosphoric oxide in a vacuum pistol (Found : C, 34·2; H, 4·7; Cu, 30·3. Calc. for $CuC_6H_{10}O_4$: C, 34·4; H, 4·8; Cu, 30·3%. Found : C, 39·5; H, 5·8; Cu, 26·8. Calc. for $CuC_8H_{14}O_4$: C, 40·4; H, 5·95; Cu, 26·7%).

Copper(II) laurate, stearate, and behenate were prepared by metathesis of alcoholic copper(II) acetate with an alcoholic solution of the appropriate acid. The resulting precipitates were washed free from excess of acid and recrystallised from dioxan. Excess of solvent was removed at 100° over phosphoric oxide in a vacuum pistol, leaving as pale blue powders the laurate (Found : C, 62·0; H, 9·9; Cu, 13·8. Calc. for $CuC_{24}H_{46}O_4$: C, 62·4; H, 10·1; Cu, 13·8%), stearate (Found : C, 67·6; H, 11·1; Cu, 10·1. Calc. for $CuC_{36}H_{70}O_4$: C, 68·6; H, 11·2; Cu, 10·1%) and behenate (Found : C, 71·0; H, 11·6; Cu, 8·46. Calc. for $CuC_{44}H_{86}O_4$: C, 71·1; H, 11·7; Cu, 8·56%). Copper was determined by electrolytic deposition on a platinum electrode.

Magnetic Measurements.—The magnetic susceptibilities of the powdered copper alkanoates were determined at room temperature by the Gouy method with a field strength of *ca.* 5000 gauss. The gram susceptibility, χ_g, the molar susceptibility, χ_M (corrected for the underlying diamagnetism of all atoms, Δ), and the magnetic moment, μ, calculated from the expression $\mu = 2{\cdot}839[(\chi_M - N\alpha)T]^{0{\cdot}5}$, are listed in Table 1. The diamagnetic correction, Δ, was measured directly on samples of the free acids, and it includes the values -13×10^{-6} for water and -17×10^{-6} for copper. A value $N\alpha = 60 \times 10^{-6}$ has been used to correct for the temperature-independent paramagnetism of bivalent copper. Copper sulphate pentahydrate was used as a calibrant for these measurements. Room-temperature data for copper(II) formate, acetate, and valerate have also been included in Table 1 for comparison.

Table 1. *Room-temperature magnetic data for copper*(II) n-*alkanoates.*

Compound	Temp. (°c)	$10^6\chi_g$	$-10^6\Delta$	$10^6\chi_M$	μ (B.M.)
$CuSO_4,5H_2O$	20·0	5·90	122	1595	1·91
$Cu(H{\cdot}CO_2)_2$	16·2	7·33	48	1174	1·61
$Cu(H{\cdot}CO_2)_2,4H_2O$	15·5	4·95	100	1218	1·64
$Cu(CH_3{\cdot}CO_2)_2$	22·2	4·39	72	869	1·39
$Cu(CH_3{\cdot}CO_2)_2,H_2O$	21·0	4·03	85	889	1·40
$Cu(C_2H_5{\cdot}CO_2)_2$	15·7	3·61	96	854	1·36
$Cu(C_2H_5{\cdot}CO_2)_2,H_2O$	17·5	3·47	109	899	1·40
$Cu(C_3H_7{\cdot}CO_2)_2$	17·2	3·14	120	866	1·37
$Cu(C_3H_7{\cdot}CO_2)_2,H_2O$	23·7	2·67	133	816	1·35
$Cu(C_4H_9{\cdot}CO_2)_2$	19·8	2·84	144	899	1·41
$Cu(C_{11}H_{23}{\cdot}CO_2)_2$	20·4	1·32	280	890	1·40
$Cu(C_{17}H_{35}{\cdot}CO_2)_2$	17·2	0·842	315	846	1·36
$Cu(C_{21}H_{43}{\cdot}CO_2)_2$	17·5	0·708	376	900	1·40

The temperature variation of the magnetic susceptibility was determined between 90° and 400° K, as described in Part I, for the propionate, butyrate, laurate, stearate, and behenate. Each sample was studied at two different field strengths between 5000 and 8000 gauss, the

TABLE 2. *Experimental gram and molar susceptibilities (c.g.s., e.m.u.) and magnetic moments* (B.M.), *at various absolute temperatures.*

Anhydrous copper propionate

Temp. (K) ...	99·0°	111·2°	125·2°	149·5°	175·2°	209·8°	225·1°	248·9°	270·0°	274·5°	298·0°	326·0°	345·3°
$10^6\chi_g$	0·741	1·09	1·50	2·29	2·83	3·30	3·44	3·61	3·63	3·61	3·53	3·60	3·42
$10^6\chi_M$	251	324	411	576	690	788	817	853	857	853	836	850	813
μ (B.M.) ...	0·390	0·496	0·595	0·789	0·943	1·11	1·17	1·26	1·32	1·33	1·40	1·44	1·45

Copper propionate monohydrate

Temp. (K) ...	97·4°	109·7°	124·8°	150·0°	169·8°	206·5°	228·8°	254·0°	270·0°	292·1°	313·3°	351·8°	374·9°
$10^6\chi_g$	0·638	1·15	1·63	2·33	2·70	3·12	3·32	3·47	3·48	3·47	3·46	3·33	3·30
$10^6\chi_M$	254	371	480	640	724	819	865	899	901	899	897	867	860
μ (B.M.) ...	0·390	0·525	0·650	0·838	0·954	1·12	1·22	1·31	1·36	1·41	1·45	1·51	1·56

Anhydrous copper butyrate

Temp. (K) ...	101·2°	111·1°	125·3°	151·5°	179·8°	212·8°	225·2°	254·7°	274·8°	289·9°	308·6°	335·0°	386·2°
$10^6\chi_g$	0·447	0·774	1·16	1·84	2·41	2·84	2·94	3·10	3·14	3·14	3·12	3·12	2·92
$10^6\chi_M$	226	304	396	558	693	795	819	857	867	867	862	862	814
μ (B.M.) ...	0·368	0·468	0·583	0·780	0·958	1·12	1·17	1·29	1·34	1·37	1·41	1·47	1·53

Copper butyrate monohydrate

Temp. (K) ...	97·8°	121·3°	144·5°	171·2°	196·4°	220·8°	246·0°	276·5°	291·2°	298·0°	305·0°	319·2°	344·3°
$10^6\chi_g$	0·294	0·856	1·36	1·87	2·19	2·42	2·56	2·65	2·66	2·68	2·68	2·65	2·60
$10^6\chi_M$	208	352	481	611	693	751	788	811	813	819	819	811	798
μ (B.M.) ...	0·342	0·534	0·700	0·872	1·00	1·11	1·20	1·29	1·33	1·35	1·37	1·39	1·43

Copper laurate

Temp. (K) ...	97·1°	111·5°	122·9°	148·5°	173·0°	224·0°	245·4°	250·0°	275·3°	301·0°	351·2°
$10^6\chi_g$	0·228	0·483	0·668	0·985	1·12	1·33	1·36	1·36	1·33	1·28	1·22
$10^6\chi_M$	385	503	589	735	798	895	909	909	895	871	845
μ (B.M.) ...	0·504	0·631	0·724	0·899	1·02	1·23	1·30	1·31	1·36	1·40	1·49

Copper stearate

Temp. (K) ...	99·3°	111·2°	124·1°	144·3°	165·3°	203·8°	224·4°	249·4°	275·0°	299·7°	323·0°	352·2°
$10^6\chi_g$	0·163	0·329	0·484	0·585	0·690	0·833	0·863	0·877	0·867	0·821	0·786	0·738
$10^6\chi_M$	418	522	620	684	750	838	859	866	862	833	810	780
μ (B.M.).....	0·535	0·644	0·749	0·852	0·959	1·13	1·20	1·28	1·35	1·37	1·40	1·43

Copper behenate

Temp. (K) ...	99·9°	110·5°	125·5°	148·8°	198·5°	224·3°	246·0°	259·7°	270·0°	283·4°	311·0°	350·0°
$10^6\chi_g$	0·114	0·218	0·333	0·445	0·614	0·680	0·702	0·710	0·712	0·710	0·690	0·652
$10^6\chi_M$	461	538	623	707	832	881	897	904	905	904	889	860
μ (B.M.) ...	0·569	0·653	0·755	0·881	1·11	1·22	1·29	1·33	1·36	1·39	1·44	1·50

mean of the two susceptibilities being taken. No evidence was obtained for dependence of susceptibility upon the strength of the magnetic field. The experimental results are contained in Table 2.

DISCUSSION

The first systematic study of the room-temperature magnetic properties of copper(II) *n*-alkanoates was made in 1938 by Amiel [3] on fourteen copper(II) salts between acetate and stearate and showed that their molar susceptibilities at 20° C lay in the range $863 \pm 33 \times 10^{-6}$ c.g.s., e.m.u., that is considerably below the value $\sim 1600 \times 10^{-6}$ c.g.s., e.m.u. usually observed for copper(II) salts. Corresponding values for the seven compounds now studied ($858 \pm 42 \times 10^{-6}$ c.g.s., e.m.u.) agree well with Amiel's values.

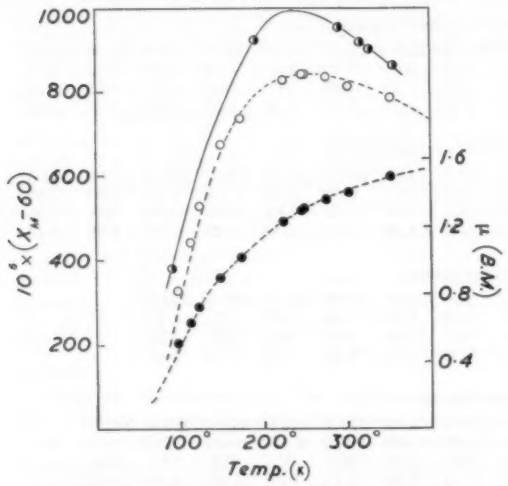
More recently, Amiel *et al.*[4] have attributed this large drop in magnetic susceptibility to the capacity of alkanoate groups to function as bidentate chelating ligands, giving rise to inner complex structures of type (II). However, they gave no indication why this

[3] Amiel, *Compt. rend.*, 1938, **207**, 1097.
[4] Amiel, Ploquin, and Dixmier, *Compt. rend.*, 1951, **232**, 2097.

structure should be associated with abnormally low susceptibilities. Obviously, chelation alone cannot quench the paramagnetism of these compounds.

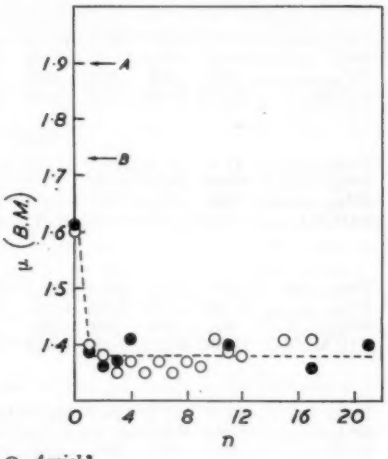
Gilmour and Pink [5] have explained the anomalous temperature-dependence of the susceptibility which they observed for copper(II) laurate (cf. Fig. 1) in terms of Amiel's covalent chelate structure (II). They proposed a crystallographic stacking of these planar molecules to form planes of copper atoms separated by the fatty acid groups extending in both directions. Intermolecular exchange interactions of an antiferromagnetic nature could then take place between the copper atoms in any plane, and lead to both the diminished susceptibility and its anomalous temperature-dependence.

FIG. 1. *Experimental and calculated magnetic susceptibilities and moments of anhydrous cupric laurate.*



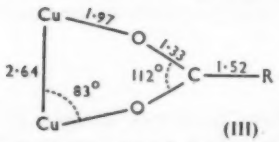
○ *Experimental susceptibility,* $10^6 \times (\chi_M - 60)$.
● *Experimental moment,* μ.
◑ *Gilmour and and Pink.*[5]
— — — *Calculated from eqn.* 6.

FIG. 2. *Experimental magnetic moments,* μ, *of anhydrous cupric* n*-alkanoates as a function of chain length* {*n in* $Cu(H\cdot[CH_2]_n\cdot CO_2)_2$}.



○ *Amiel.*[3]
● *Present work.*
A, Value usually observed for copper(II) *compounds.*
B, "Spin-only" value for copper(II) *compounds.*

If this hypothesis is correct, the magnetic moments of copper(II) *n*-alkanoates should vary with increasing length of the *n*-alkyl chains, steric hindrance between adjacent chains leading to greater separation, and consequently to smaller intermolecular exchange interactions, between contiguous copper atoms. That this is not so can be seen from the variation of magnetic moment with chain length, illustrated in Fig. 2. A striking feature of the curve is the uniform quenching of magnetic moment, the values for all anhydrous alkanoates, with the exception of the formate, lying in the narrow region 1·38 ± 0·03 B.M.



(III)

The marked independence of magnetic moment on length of the *n*-alkyl chain suggests that the magnetic anomaly has the same origin in all copper alkanoates between acetate and behenate, and this in turn implies that their molecular structures are closely similar. A binuclear structure has already been unambiguously established for copper acetate by Niekerk and Schoening,[2] and it is therefore suggested that all the higher homologues should be similarly formulated as the carboxylate-bridged binuclear inner complexes,

[5] Gilmour and Pink, *J.*, 1953, 2198.

$[Cu_2(R{\cdot}CO_2)_4(H_2O)_{0\text{ or }2}]$, shown in (I). The five-membered Cu–O–C–O–Cu rings, illustrated with dimensions (Å) from ref. 2 for R = Me in (III), would be expected on steric grounds to be more stable than the four-membered Cu–O–C–O rings suggested by Amiel. Furthermore, since the dimensions of a carboxylate bridge are unlikely to be influenced by the length of the attached *n*-alkyl group, the copper–copper distance will be maintained close to the value 2·64 Å as in the acetate. It follows that the copper–copper intramolecular exchange interactions will also show little variation with chain length, and hence the magnetic properties of all homologues will be closely similar.

The susceptibility–temperature curves for these compounds are, in fact, remarkably similar. For each compound the susceptibility rises steeply from zero with increasing temperature, passes through a broad maximum in the region 278° ± 28° K, and then decreases with further increase in temperature (cf. Fig. 1). This characteristic shape of the χ–T curves reflects the thermal distribution of binuclear copper *n*-alkanoate molecules between a lower singlet (diamagnetic) and an upper triplet (paramagnetic) level as described in Part I. At 0° K, the binuclear molecules are in singlet states ($S = 0$), and make no contribution to the paramagnetic susceptibility. As the temperature is raised, the triplet level ($S = 1$) becomes increasingly populated at the expense of the singlet level and the susceptibility rapidly increases. In the region of 278° K Curie-law behaviour becomes dominant, the susceptibility passing through a maximum and then decreasing as the temperature is further raised.

This behaviour is remarkably well represented by the general expression * derived in Part I:

$$\chi_M = \frac{g^2N\beta^2}{3kT}[1 + 1/3 \exp(J/kT)]^{-1} + N\alpha \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where χ_M is the magnetic susceptibility per mole of copper atoms, g is the spectroscopic splitting factor, β is the Bohr magneton, J is the energy interval between the singlet and triplet levels, and $N\alpha$ is a small temperature-independent paramagnetic contribution to the susceptibility. If, to a first approximation, J is assumed to be temperature-independent, differentiation of eqn. (1) leads to the result $J = 1{\cdot}6kT_c$, where T_c is the temperature at which the susceptibility attains its maximum value. For the present compounds, the splitting factor, g, has been estimated by substituting the experimental value of the susceptibility, at the arbitrary temperature T_c, into eqn. (1). The resulting susceptibility equations (curve in Fig. 1) are:

$Cu(C_2H_5{\cdot}CO_2)_2$: $10^6 \times \chi_M = (0{\cdot}571/T)[1 + 1/3 \exp(432/T)]^{-1} + 60$ (2)

$Cu(C_2H_5{\cdot}CO_2)_2,H_2O$: $10^6 \times \chi_M = (0{\cdot}602/T)[1 + 1/3 \exp(432/T)]^{-1} + 60$ (3)

$Cu(C_3H_7{\cdot}CO_2)_2$: $10^6 \times \chi_M = (0{\cdot}621/T)[1 + 1/3 \exp(464/T)]^{-1} + 60$ (4)

$Cu(C_3H_7{\cdot}CO_2)_2,H_2O$: $10^6 \times \chi_M = (0{\cdot}614/T)[1 + 1/3 \exp(488/T)]^{-1} + 60$ (5)

$Cu(C_{11}H_{23}{\cdot}CO_2)_2$: $10^6 \times \chi_M = (0{\cdot}563/T)[1 + 1/3 \exp(400/T)]^{-1} + 60$ (6)

$Cu(C_{17}H_{35}{\cdot}CO_2)_2$: $10^6 \times \chi_M = (0{\cdot}536/T)[1 + 1/3 \exp(400/T)]^{-1} + 60$ (7)

$Cu(C_{21}H_{43}{\cdot}CO_2)_2$: $10^6 \times \chi_M = (0{\cdot}605/T)[1 + 1/3 \exp(432/T)]^{-1} + 60$ (8)

The agreement between the experimental results and these equations is unexpectedly good in view of the assumption of a temperature-independent value of J, and other assumptions made in the derivation of equation (1) (cf. Part I).

* In Part I, in equations (1) and (2), the symbol N should be replaced by $N/2$, *i.e.*, the number of very weak covalent copper–copper bonds formed by N copper atoms.

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The close similarity in the magnetic properties of these compounds and those of binuclear copper acetate is further emphasised by the comparison of corresponding values for T_c, g, and J given in Table 3.

TABLE 3. *Comparison of T_c, g, and J for copper*(II) n-*alkanoates.*

Compound	T_c°, K	g	J cm.$^{-1}$	J kcal. mole^{-1}
$Cu(CH_3 \cdot CO_2)_2$	270	2·17	300	0·86
$Cu(CH_3 \cdot CO_2)_2, H_2O$	255	2·13	284	0·82
$Cu(C_3H_5 \cdot CO_2)_2$	270	2·14	300	0·86
$Cu(C_3H_5 \cdot CO_2)_2, H_2O$	270	2·20	300	0·86
$Cu(C_3H_7 \cdot CO_2)_2$	290	2·23	322	0·92
$Cu(C_3H_7 \cdot CO_2)_2, H_2O$	305	2·22	339	0·97
$Cu(C_{11}H_{23}CO_2)_2$	250	2·12	278	0·79
$Cu(C_{17}H_{35}CO_2)_2$	250	2·07	278	0·79
$Cu(C_{21}H_{43} \cdot CO_2)_2$	270	2·20	302	0·86

For all the compounds, including the acetate, these quantities lie in the following narrow ranges: $T_c = 278° \pm 28°$ K; $g = 2·15 \pm 0·08$; $J = 309 \pm 31$ cm.$^{-1}$ $= 0·88 \pm 0·09$ kcal. mole^{-1}. It must be stressed that these ranges include appreciable experimental scatter, first on account of the inherent difficulty in reproducing the packing of powdered samples in Gouy tubes, and secondly owing to the difficulty in selecting a value for T_c from such broad maxima as are exhibited by the χ–T curves. Even so, these results amply confirm that the length of the *n*-alkyl chain has no significant effect on the magnetic properties of these compounds. It is concluded that while only *X*-ray analysis can unequivocally establish the structure of these salts, the remarkable uniformity in their magnetic properties leaves little reason to doubt that their molecular structures are fundamentally identical and similar to that of copper acetate.

Although supporting crystallographic data are, at present, not available for alkanoates higher than the acetate, other evidence favouring a binuclear structure for these compounds has recently been published. For example, crystalline copper(II) propionate displays anomalous paramagnetic absorption of microwaves identical with that of copper acetate.[6] Furthermore, the polarised absorption spectra of these two compounds, in the visible and near-ultraviolet regions, are closely similar, each exhibiting a new kind of absorption band at 3750 Å not previously observed in the spectra of copper(II) compounds.[7] This band has been tentatively ascribed [7] to a direct linkage between copper atoms in these compounds, and in conjunction with the present data, indicates that the propionate, at least, adopts a binuclear configuration.

It was suggested in Part I that the small increase in J of 16 cm.$^{-1}$ observed on dehydration of copper acetate might be real, reflecting an increased $3d_{z^2}$–$3d_{z^2}$ overlap resulting from the removal of the two terminal water molecules. This possibility is not confirmed by the data for the propionate and butyrate in Table 3, the experimental scatter of J values over the range, 309 ± 31 cm.$^{-1}$, being too great to permit the detection of an effect of this small order of magnitude.

The magnetic properties of copper(II) formate remain, at present, unexplained. The room-temperature moment of the powdered hydrated or anhydrous salt, $\mu \sim 1·6$ B.M., is intermediate between the value $\mu = 1·38$ B.M. consistently observed for its homologues and the value $\mu = 1·9$ B.M. observed for magnetically dilute copper(II) compounds. This partial reduction in moment cannot be explained by intramolecular exchange forces of the present type, for a crystal-structure determination [8] of the tetrahydrate has shown that each copper atom is surrounded by four oxygen atoms from four different formate groups, in an approximately square configuration, and by two water molecules at a greater

[6] Abe, *Phys. Rev.*, 1953, **92**, 1572.
[7] Tsuchida and Yamada, *Nature*, 1955, **176**, 1171.
[8] Kiriyama, Ibamoto, and Matsuo, *Acta Cryst.*, 1954, **7**, 482.

distance to complete a distorted CuO_6 octahedron. In aqueous solution [9] the moment jumps from 1·6 to 1·9 B.M., which suggests that strong intermolecular exchange forces are present in the crystalline compound. This conclusion is supported by the paramagnetic resonance absorption of microwaves by the tetrahydrate [10] which, while displaying no marked anomalies, does indicate the presence of appreciable exchange interactions. Their existence is also reflected in a large value of the Weiss constant, $\theta = -150°$, for the tetrahydrate.[11] These results will be reported later.

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[9] Martin and Whitley, unpublished experiments.
[10] Lancaster and Gordy, *J. Chem. Phys.*, 1951, **19**, 1181.
[11] Martin and Waterman, unpublished experiments.

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496. *The Parachors of the Alkanes.*

By D. J. G. Ives and A. McM. Taylor.

A statistical comparison has been made between the parachors of branched-chain and normal alkanes in order to evaluate parachor increments attributable to various interactions between non-bonded atoms. This is shown to lead to a simple and accurate method of correlating the parachors of these compounds. Comments are made upon the significance of the parachor and upon its dependence upon molecular structure.

The effects of interactions between non-bonded atoms upon the parachors of the alkanes have been studied by making an *ad hoc* statistical comparison of the observed parachors of normal and of branched-chain isomerides. For this purpose, it has been assumed that the parachor of a given alkane is the sum of atomic constants and of increments due to the interactions associated with certain molecular structural factors. Thus:

$$[P] \text{ for } C_nH_{2n+2} = n[P]_C + (2n + 2)[P]_H + n_a p_a + n_b p_b + \quad . \quad . \quad (1)$$

where the structural factor, a, giving rise to a parachor increment p_a, occurs n_a times within the molecule, and so on. Subtraction of the parachors of a set of branched-chain, isomeric alkanes from the parachor of the normal isomeride provides a set of differences, each one of which may be represented.

$$\Delta[P] = (n_a^n - n_a^b)p_a + (n_b^n - n_b^b)p_b + \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where the superscripts indicate " normal " and " branched."

Although each difference is comparatively small, and correspondingly sensitive to experimental error, a sufficient number of them can be used statistically to determine values for the structural increments, p_a, p_b, etc., with some reliability. This has been done by applying the method of least squares, the required values of the increments being taken as those which minimised the over-all sum of the squares of the residual deviations between calculated and observed values of $\Delta[P]$. Data from the literature,[1] recalculated where necessary, have been used to provide a set of 28 parachor differences, to which this treatment has been applied.

[1] Coffin and Maass, *J. Amer. Chem. Soc.*, 1928, **50**, 1427; Timmermans, Hennaut-Roland, *et al.*, *J. Chim. phys.*, 1926, **23**, 733; 1928, **25**, 411; 1932, **29**, 529; 1935, **32**, 501; *Bull. Soc. chim. belges*, 1931, **40**, 177; Wibaut, Hoog, Langedijk, Overhoff, and Smittenberg, *Rec. Trav. chim.*, 1939, **58**, 329; Quayle, Day, and Brown, *J. Amer. Chem. Soc.*, 1944, **66**, 938; Edgar and Calingaert, *ibid.*, 1929, **51**, 1540; Richards, Speyers, and Carver, *ibid.*, 1924, **46**, 1196; Vogel, *J.*, 1946, 133.

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Since the parachor increments to be evaluated are hypothetically attributed to interactions between atoms not directly bound to each other by valency bonds, it was considered that no interactions between atoms outside a " three-carbon group " could be significant. That is to say, only those interactions occurring between any pair of non-bonded atoms in a chain of three carbon atoms, with their attached hydrogen atoms, were taken into account. Some of these were found by trial not to be significant. The method may be illustrated in terms of the interactions listed in Table 1.

TABLE 1.

Interactions between :	Symbol
Next-but-one carbon atoms,	c_1
H atoms linked to the same C,	h_1
Methyl H atoms and H on adjacent C,	h_{2a}
H atoms on adjacent methylenes, $-CH_2 \cdot CH_2-$	h_{2b}
H atoms of adjacent methylene and methine,	h_{2c}
H atoms of adjacent methines,	h_{2d}
H atoms on adjacent C atoms, undifferentiated ($\Sigma[h_{2a}/3,\ h_{2b}/4,\ h_{2c}/2,\ h_{2d}]$)	h_2
H atoms on C atoms once removed,	h_3
C atom and H on adjacent C,	ch_1
C atom and H on C atom once removed,	ch_2

The number of times a structural factor which gives rise to a particular kind of interaction occurs in a branched-chain alkane is subtracted from the number of times it occurs in the corresponding normal isomeride, giving a coefficient of one of the parachor increments in equation (2). All of these coefficients, for the alkanes indicated, are collected in Table 2, together with the values of $\Delta[P]$ adopted for the calculations.

It will be noticed that the coefficients of the factors c_1, h_1, and ch_1 are invariably in the ratio $1 : 1 : -2$. This is a necessary relation similar to that noted by Gibling [2] which compels the use of a composite structural factor, $(c_1 + h_1 - 2ch_1)$.

In order to determine which of the factors were significant, the least-squares calculation was performed a number of times. In the first calculation, none of the factors was considered: in the second, $(c_1 + h_1 - 2ch_1)$ alone was taken into account; in subsequent trials of this kind, the other factors were introduced progressively and, where reasonable, alternatively. In each case, the root mean square deviation between observed and calculated values of $\Delta[P]$ gave a measure of closeness of fit. Those interactions whose introduction improved the closeness of fit were considered to be significant; those which gave no improvement were discarded as insignificant. A selection of the results of these trials is shown in Table 3.

It appears that differentiation of interactions between hydrogen atoms on adjacent carbon atoms (*i.e.*, subdivision of h_2 into $h_{2a} \ldots h_{2d}$) is warranted, notwithstanding that

[2] Gibling, *J.*, 1945, 236.

the corresponding increments stand nearly in proportion to the number of combinations in pairs of hydrogen atoms which are involved. The inclusion of an interaction between hydrogen atoms attached to carbon atoms once removed (h_3) is justified, but its subdivision is not. The increment is small, but its coefficients are large. The zero increment for ch_2 which has been found is to be expected. It will be noticed that all the increments are negative and fall away rapidly with increasing distance between the interacting atoms. The values shown in the last line of Table 3 have been adopted.

TABLE 2.

Alkane	Coefficients										
	c_1	h_1	h_2	h_{2a}	h_{2b}	h_{2c}	h_{2d}	h_3	ch_1	ch_2	$\Delta[P]$
*iso*Butane	1	1	− 7	−1	−1	0	0	15	−2	8	− 0·1
*iso*Pentane	1	1	− 6	0	−2	1	0	8	−2	6	− 1·15
2-Methylpentane	1	1	− 6	0	−2	1	0	9	−2	6	− 1·5
3-Methylpentane	1	1	− 5	1	−3	2	0	2	−2	4	− 3·0
2 : 2-Dimethylbutane	3	3	−18	−2	−3	0	0	25	−6	18	− 4·3
2 : 3-Dimethylbutane	2	2	−11	0	−3	0	1	10	−4	10	− 4·5
2-Methylhexane	1	1	− 6	0	−2	1	0	9	−2	6	− 1·7
3-Methylhexane	1	1	− 5	1	−3	2	0	3	−2	4	− 4·3
3-Ethylpentane	1	1	− 4	2	−4	3	0	−3	−2	2	− 7·1
2 : 2-Dimethylpentane	3	3	−18	−2	−3	0	0	27	−6	18	− 4·95
2 : 3-Dimethylpentane	2	2	−10	1	−4	1	1	5	−4	8	− 7·15
2 : 4-Dimethylpentane	2	2	−12	0	−4	2	0	19	−4	12	− 4·45
3 : 3-Dimethylpentane	3	3	−16	0	−4	0	0	13	−6	14	− 7·15
2 : 2 : 3-Trimethylbutane	4	4	−22	−2	−4	0	0	21	−8	20	− 8·8
2-Methylheptane	1	1	− 6	0	−2	1	0	9	−2	6	− 1·85
3-Methylheptane	1	1	− 5	1	−3	2	0	3	−2	4	− 3·3
4-Methylheptane	1	1	− 5	1	−3	2	0	4	−2	4	− 3·5
3-Ethylhexane	1	1	− 4	2	−4	3	0	−2	−2	2	− 6·1
2 : 3-Dimethylhexane	2	2	−10	1	−4	1	1	6	−4	8	− 6·6
2 : 5-Dimethylhexane	2	2	−12	0	−4	2	0	18	−4	12	− 4·0
3 : 4-Dimethylhexane	2	2	− 9	2	−5	2	1	0	−4	6	− 8·2
2 : 2 : 3-Trimethylpentane	4	4	−21	−1	−5	1	0	17	−8	18	−10·2
2 : 2 : 4-Trimethylpentane	4	4	−24	−2	−5	1	0	38	−8	24	− 6·9
3-Ethyl-3-methylpentane	3	3	−14	2	−5	0	0	2	−6	10	−10·6
2 : 6-Dimethylheptane	2	2	−12	0	−4	2	0	18	−4	12	− 4·2
2 : 7-Dimethyloctane	2	2	−12	0	−4	2	0	18	−4	12	− 4·3
4 : 5-Dimethyloctane	2	2	− 9	2	−5	2	1	2	−4	6	−10·5
3 : 4-Diethylhexane	2	2	− 7	4	−7	4	1	−8	−4	2	−12·9

TABLE 3.

Interactions considered	Parachor increments								Residual deviation, r.m.s.
	$c_1 + h_1 - 2ch_1$	h_2	h_{2a}	h_{2b}	h_{2c}	h_{2d}	h_3	ch_2	
No interactions	—	—	—	—	—	—	—	—	6·31
$(c_1 + h_1 - 2ch_1)$ only	− 2·6	—	—	—	—	—	—	—	2·66
$(c_1 + h_1 - 2ch_1)$, h_2	−12·4	−1·8	—	—	—	—	—	—	0·90
$(c_1 + h_1 - 2ch_1)$, h_{2a}, h_{2b}, h_{2c}, h_{2d}	− 9·8	—	−4·3	−5·5	−3·2	−1·9	—	—	0·56
$(c_1 + h_1 - 2ch_1)$, h_2, h_3	−23·9	−4·4	—	—	—	—	−0·45	—	0·69
$(c_1 + h_1 - 2ch_1)$, h_{2a}, h_{2b}, h_{2c}, h_{2d}, h_3	−15·9	—	−8·3	−10·8	−5·7	−3·1	−0·2	—	0·50
$(c_1 + h_1 - 2ch_1)$, h_{2a}, h_{2b}, h_{2c}, h_{2d}, h_3, ch_2	−15·9	—	−8·3	−10·8	−5·7	−3·1	−0·2	0	0·50

Once the parachor increments have been determined in this way, they can be applied to individual compounds to eliminate the effects of all interactions which are not common to a set of isomerides. Thus, a corrected parachor, $[P]'$, may be obtained by subtracting the appropriate numbers of structural increments from the observed parachor of a compound. This gives, not a summation of atomic parachors alone, but the parachor of a hypothetical alkane in which all the hydrogen–hydrogen interactions are removed except

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those which are present in methane, and all the carbon–hydrogen interactions except those of the kind which occur in ethane. This may be expressed as

$$[P]' = n[P]_C + (2n + 2)[P]_H + 6h_1 + 6(n - 1)ch_1 \quad . \quad . \quad . \quad . \quad (3)$$

This quantity is found in fact to be linear with n; the least-squares line for the 28 branched-chain alkanes and their 7 normal isomerides passes through the origin with negligible error and is represented by:

$$[P]' = 67{\cdot}34n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

All alkanes with the same value of n should have the same value of $[P]'$. This requirement has been tested, for all the original 35 alkanes and all the additional members of the series for which Quayle [3] has collected data. The results of this test are shown in Table 4, together with the predictions of equation (4).

For 60 hydrocarbons from ethane to hexadecane, the mean deviation between observed and calculated values of $[P]'$ is 0·07% and for 53 of these it is 0·04%. One C_8 hydrocarbon (3-ethyl-2-methylpentane) and five C_9 hydrocarbons (2 : 2 : 4 : 4-tetramethylpentane, 2 : 2 : 4-trimethylhexane, 2 : 3-, 2 : 4-, and 3 : 3-dimethylheptane) show much wider deviations, between 0·4% and 2%; four of the discrepant results rest on unsupported observations. Increased deviations occur for extreme values of n and may be associated

TABLE 4.

n	No. of isomers	Obs. or mean of obs. $[P]'$	Mean deviatn. from mean (%)	Calc. $[P]'$ eqn. (4)	Obs. − calc. $[P]'$ (%)
1	1	72·6	—	67·3	+7·30
2	1	135·4	—	134·7	+0·52
3	1	199·9	—	202·0	−1·10
4	2	268·95	0·56	269·4	−0·17
5	2	337·0	0·06	336·7	+0·09
6	5	404·0	0·12	404·0	0·00
7	9	471·4	0·08	471·4	0·00
8	16	539·1	0·07	538·7	+0·07
9	12	605·9	0·06	606·1	−0·03
10	5	673·1	0·11	673·4	−0·04
11	2	740·7	0·05	740·7	0·00
12	1	808·5	—	808·1	+0·05
13	1	876·2	—	875·4	+0·09
14	1	944·6	—	942·8	+0·19
15	1	1012	—	1010	+0·20
16	1	1079	—	1078	+0·09
26	1	1765	—	1751	+0·79
32	1	2170	—	2155	+0·69
60	1	4114	—	4040	+2·04

TABLE 5.

$67{\cdot}34n$	$(c_1 + h_1 - 2ch_1)$	h_{2a}	h_{2b}	h_{2c}	h_{2d}	h_3	$[P]_{calc.}$	$[P]_{obs.}$
n-Octane								
	6	4	5	0	0	28		
538·7	− 95·4	−33·2	−54·0	—	—	− 5·6	350·5	351·2
2 : 2 : 3-Trimethylpentane								
	10	3	0	1	0	45		
538·7	−159·0	−24·9	—	−5·7	—	− 9·0	340·1	340·3
2 : 3 : 3-Trimethylpentane								
	10	4	0	0	0	38		
538·7	−159·0	−33·2	—	—	—	− 7·6	338·9	339·0
2 : 3 : 4-Trimethylpentane								
	9	5	0	0	2	37		
538·7	−143·1	−41·5	—	—	−6·2	− 7·4	340·5	340·8
2 : 2 : 4-Trimethylpentane								
	10	2	0	1	0	66		
538·7	−159·0	−16·6	—	−5·7	—	−13·2	344·2	343·7

[3] Quayle, *Chem. Rev.*, 1953, **53**, 439.

with " first-term anomalies " and with the " hexadecyl discontinuity " discussed by Mumford.[4]

Equation (4), and the six interaction increments, provide one of the best means of correlating the parachors of the alkanes from C_4 to C_{16}. An example is given in Table 5 of the calculation of the parachors of five C_8 hydrocarbons, the results being compared with the observed parachors given by Quayle.[3]

It is clear that, for all four of the trimethylpentanes, the variation of the parachor with the positions of the methyl groups is adequately expressed.

Discussion

The correspondence between parachors and molecular volumes has recently been demonstrated.[5] It is probable that close proportionality depends on uniformity of intermolecular forces and on the absence of preferred molecular orientation at the liquid surface. These conditions are likely to be satisfied by non-polar molecules which are not too long and attract each other by means of dispersion forces only. The analysis of the alkane data, and recent applications of the parachor to studies of preferred conformations of alkoxide molecules,[6] support this opinion.

Applications of the parachor depending on its division into additive structural and atomic constants must always be uncertain because of the arbitrary assumptions necessarily involved in such a division.[7] The concept of an atomic constant is difficult to accept, since, for atoms which define the size of the molecular skeleton, covalent radii will be significant parameters, whereas for peripheral atoms van der Waals dimensions will apply. Interactions between non-bonded atoms complicate the task and may arise in different ways. Normally, they are considered in terms of overlap of van der Waals fields and may greatly affect molecular volume in cases such as the perfluoroalkanes, where significant interpenetration is prevented.[8] It is, however, necessary to consider the envelope volumes generated by librational or rotational motion of molecules in the liquid phase. In attempting to divide such a volume into atomic contributions, the difficulty is encountered that one atom may follow the rotational path of another and so require no additional space in which to execute its own motion. Thus, in a hypothetical, freely rotating methyl group, all three hydrogen atoms traverse the same path which could equally well be swept out by one of them. Such coincidences will produce an effective " loss of volume " in a summation of atomic constants, and it is suggested that this effect is of predominant importance.

The alkane data may be examined in the light of these considerations. In equation (3) $[P]_O$ is a function of the covalent radius of carbon; $[P]_H$ is a function of the van der Waals radius of hydrogen, and the interaction ch_1 is probably zero in effect. If this is so, equation (3), with $n = 0$, requires:

$$2[P]_H + 6h_1 = 0$$

The residual interaction effects, $6h_1$, are those present in methane, and the " loss in volume " due to them can be identified with the " volume " of two hydrogen atoms, since a hypothetical, rotating CH_2 molecule would generate the same envelope volume as a rotating methane molecule. Whether this result is coincidental or not, a case has been made that, in the alkane series, the parachor is a very well behaved molecular function of real physical significance.

The authors record their respect and gratitude to the late Professor S. Sugden, F.R.S., from whose encouragement and advice both derived great benefit.

Birkbeck College, London, W.C.1. [*Received, January 18th*, 1957.]

[4] Mumford, *J.*, 1952, 4897.
[5] Edward, *Chem. and Ind.*, 1956, 774.
[6] Bradley, Kay, and Wardlaw, *J.*, 1956, 4916.
[7] Samuel, *J. Chem. Phys.*, 1944, **12**, 167.
[8] Simons and Dunlap, *ibid.*, 1950, **18**, 335; Simons and Hickman, *J. Phys. Chem.*, 1952, **56**, 420.

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497. *Studies in Pyrolysis. Part X.* Model Systems for the Pyrolysis of Poly(ethylene Terephthalate): 2-Hydroxyethyl Benzoate and Related Substances.*

By H. V. R. Iengar and P. D. Ritchie.

2-Hydroxyethyl (or 2-chloroethyl) benzoate breaks down thermally in the vapour phase by three competitive primary reactions: (i) disproportionation to ethylene dibenzoate and ethylene glycol (or 1 : 2-dichloroethane): (ii) disproportionation to benzoic anhydride and diethylene glycol (or 2 : 2′-dichlorodiethyl ether); and (iii) alkyl–oxygen scission to benzoic acid and acetaldehyde (or vinyl chloride). These reactions are compared with analogous competitive scissions of 2-phenoxyethanol and 2-phenoxyethyl acetate; the pyrolysis of phenyl vinyl ether is also described. The results assist in interpreting the thermal breakdown of poly(ethylene terephthalate).

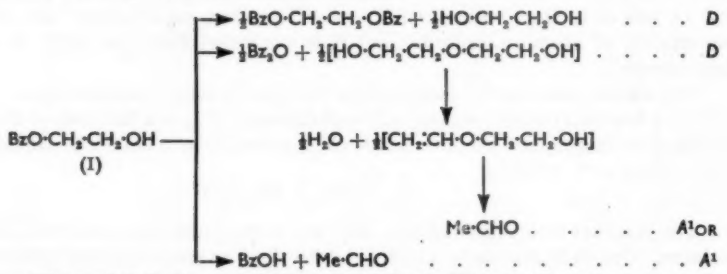
2-Hydroxyethyl benzoate (I), previously suggested [1] as a suitable model compound for studying the thermal breakdown of a terminal chain-segment of poly(ethylene terephthalate) (II), has now been pyrolysed under various conditions, and its behaviour compared with that of a number of analogous compounds.

(I) BzO·CH$_2$·CH$_2$·OH (II) H·[*p*-O$_2$C·C$_6$H$_4$·CO$_2$·CH$_2$·CH$_2$]$_n$·OH

2-Hydroxyethyl Benzoate (I).—The work has confirmed and considerably extended Cretcher and Pittenger's observation [2] that 2-hydroxyethyl esters of aromatic acids disproportionate on distillation as follows with concurrent formation of some water:

$$Ar\cdot CO_2\cdot CH_2\cdot CH_2\cdot OH \longrightarrow \tfrac{1}{2}Ar\cdot CO_2\cdot CH_2\cdot CH_2\cdot O_2C\cdot Ar + \tfrac{1}{2}HO\cdot CH_2\cdot CH_2\cdot OH$$

It has been found that although 2-hydroxyethyl benzoate can be distilled unchanged under reduced pressure, at higher temperatures it yields a range of products (including the key substance acetaldehyde, not recorded by Cretcher and Pittenger [2]) best interpreted by the following scheme of concurrent competitive reactions:


BzO·CH2·CH2·OH
(I)
½BzO·CH2·CH2·OBz + ½HO·CH2·CH2·OH . . . D
½Bz2O + ½[HO·CH2·CH2·O·CH2·CH2·OH] . . . . D
½H2O + ½[CH2:CH·O·CH2·CH2·OH]
Me·CHO A1OR
BzOH + Me·CHO A1

(The symbols D, A^1_{OR}, and A^1 have been defined previously.[1,3])

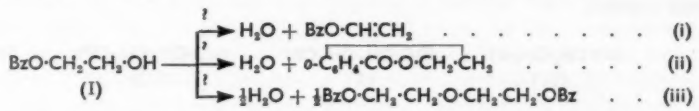
Disproportionation (*D*) of two types predominates at lower temperatures (*e.g.*, during distillation, or in the vapour phase at *ca.* 375°), though it still occurs to some extent at higher temperatures; but at *ca.* 500° alkyl–oxygen scission (A^1), which does not occur measurably at *ca.* 375°, predominates strongly, with formation of much benzoic acid (not accompanied by vinyl benzoate or its scission products, and hence not arising by the known A^1 scission of ethylene dibenzoate [1]). This effect of temperature is at first sight

* Part IX, *J.*, 1957, 2107.

[1] Allan, Forman, and Ritchie, *J.*, 1955, 2717.
[2] Cretcher and Pittenger, *J. Amer. Chem. Soc.*, 1925, **47**, 2560.
[3] Iengar and Ritchie, *J.*, 1956, 3563.

surprising, since the hydroxy-ester (I) possesses the structural feature so frequently associated with an easy A^1 scission, namely, the presence of one or more β-hydrogen atoms. It may be that the polar β-hydroxyl substituent causes the β-hydrogen atoms to be more strongly bonded to carbon, so that A^1 scission here requires a high activation energy.

A more puzzling feature of the pyrolysis of 2-hydroxyethyl benzoate is the very ready evolution of small quantities of water (even in the early stages of a simple distillation). There are various formally possible sources of this water, such as the three following direct dehydrations, of which (i) and (ii) are intramolecular, and (iii) intermolecular :

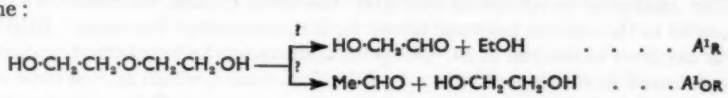


Reaction (i) at first seems likely, in view of Vaughn's claim [4] that the analogous ester 2-hydroxyethyl acetate yields, *inter alia*, water and vinyl acetate on pyrolysis; but all three reactions are here ruled out by the absence of the appropriate scission product from the low-temperature pyrolysate.

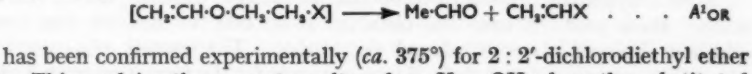
Two other possible sources of the water remain, and merit fuller consideration. In the first place, disproportionation of the benzoate (I) yields ethylene dibenzoate and ethylene glycol, and it is known [5] that at *ca.* 500° the latter yields water and acetaldehyde. However, it has been found that at *ca.* 375°, in the vapour phase, the glycol is largely unchanged, yielding only a very small amount of water (much less than that formed from 2-hydroxyethyl benzoate at this temperature).

The only reasonable alternative is a disproportionation of 2-hydroxyethyl benzoate to benzoic anhydride and diethylene glycol, followed by breakdown of the latter. This is suggested by the fact that at *ca.* 375° the ester (I) yields benzoic anhydride, but not the benzoic acid which would be expected to accompany the anhydride if the latter arose from ethylene dibenzoate by the A^1/D sequence described by Allan, Jones, and Ritchie.[6] The concept is further supported by the observation that diethylene glycol is markedly less thermostable than ethylene glycol, yielding water and acetaldehyde quite readily in the vapour phase at *ca.* 375°.

The latter observation is surprising, for it is known [7] that, in general, saturated aliphatic ethers break down thermally by $A^1{}_R$ scission; and neither this nor the alternative type of alkyl–oxygen scission $A^1{}_{OR}$ (which in any case is not known to occur for such ethers) can satisfactorily account for the observed products from diethylene glycol, as is clear from the following scheme :



It can only be supposed that the presence of negative 2 : 2′ substituents X in an aliphatic ether (III) induces thermal breakdown as shown below, the second stage being supported by previous observations [3] on the pyrolysis of alkyl vinyl ethers :



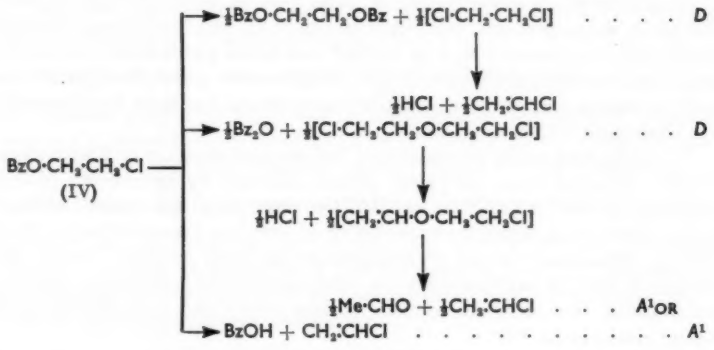
This sequence has been confirmed experimentally (*ca.* 375°) for 2 : 2′-dichlorodiethyl ether (III; X = Cl). This explains the present results, where X = OH; here the substituted olefin $CH_2{:}CHX$ is the enol of acetaldehyde.

[4] Vaughn, U.S.P. 2,415,378/1947.
[5] Nef, *Annalen*, 1904, **335**, 200.
[6] Allan, Jones, and Ritchie, *J.*, 1957, 524.
[7] Hurd, "The Pyrolysis of Carbon Compounds," Chemical Catalog Co., New York, 1929, Chap. 8.

In view of the frequency with which disproportionation has been observed in this and cognate work,[1,3,8] various analogues of 2-hydroxyethyl benzoate have been studied, partly to determine some of the structural features promoting disproportionation, and partly to confirm that the foregoing interpretation of its pyrolysis is correct. The compounds studied were the ester 2-chloroethyl benzoate (IV), the ether 2-phenoxyethanol (V), and the ether-ester 2-phenoxyethyl acetate (VI); in these the terminal groups of 2-hydroxyethyl benzoate are replaced by other simple groups of similar polarity. Phenyl vinyl ether (VII), which is related to 2-phenoxyethanol (V) and its acetate (VI), has also been studied.

$BzO{\cdot}CH_2{\cdot}CH_2{\cdot}Cl$	$PhO{\cdot}CH_2{\cdot}CH_2{\cdot}OH$	$AcO{\cdot}CH_2{\cdot}CH_2{\cdot}OPh$	$PhO{\cdot}CH{:}CH_2$
(IV)	(V)	(VI)	(VII)

2-Chloroethyl Benzoate (IV).—Bilger and Hibbert[9] have shown that 2-chloroethyl acetate yields acetic acid and vinyl chloride on pyrolysis, and it has now been found that the analogous benzoic ester (IV) also undergoes A^1 scission as one of several competitive breakdown routes at 450—500°, thus:


½BzO·CH₂·CH₂·OBz + ½[Cl·CH₂·CH₂Cl] . . . . . D
½HCl + ½CH₂:CHCl
½Bz₂O + ½[Cl·CH₂·CH₂·O·CH₂·CH₂Cl] . . . . . D
BzO·CH₂·CH₂·Cl
(IV)
½HCl + ½[CH₂:CH·O·CH₂·CH₂Cl]
½MeCHO + ½CH₂:CHCl . . . A¹OR
BzOH + CH₂:CHCl . . . . . A¹

As in several other related pyrolyses studied recently,[3,8] the pyrolysate is complex, and more than one formally possible reaction scheme can be devised to account for it; the above scheme, based partly on the present results and partly on their correlation with other analogous pyrolyses, is probably the most reliable interpretation. It is precisely parallel to the scheme proposed above for 2-hydroxyethyl benzoate. Ethylene dibenzoate was obtained in one run at *ca.* 400° (thus confirming the first *D* route), though it could not be detected in subsequent runs; 1 : 2-dichloroethane, which should have accompanied it, was not detected, though its known pyrolysis products[10] hydrogen chloride and vinyl chloride were identified. (The scheme suggests other possible sources of these, however; and 1 : 2-dichloroethane, pyrolysed under the same conditions, was observed to break down only to the extent of *ca.* 7%.) Benzoic anhydride is most probably attributable to the second *D* route, just as was deduced for the ester (I).

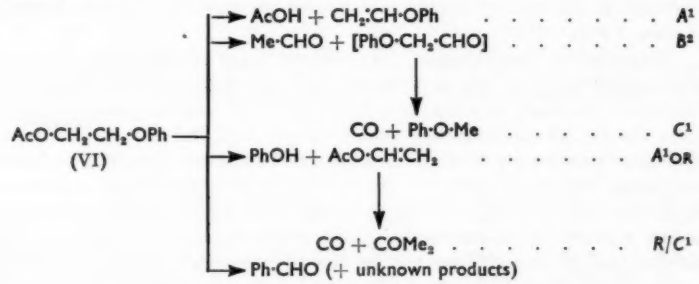
2-Phenoxyethanol (V).—This compound at *ca.* 500° yielded phenol, acetaldehyde, and water; these products were also obtained at *ca.* 600° by Knights and Cooper,[11] who in addition observed traces of phenyl vinyl ether. The normal A^1_{OR} scission of an alkyl phenyl ether to phenol and olefin[12] here accounts for the formation from 2-phenoxyethanol

[8] Allan, Iengar, and Ritchie, *J.*, 1957, 2107.
[9] Bilger and Hibbert, *J. Amer. Chem. Soc.*, 1936, **58**, 823.
[10] Barton and Howlett, *J.*, 1949, 155; Howlett, *Trans. Faraday Soc.*, 1952, **48**, 25.
[11] Knights, personal communication, 1956.
[12] Bamberger, *Ber.*, 1896, **19**, 1818; Hart and Eleuterio, *J. Amer. Chem. Soc.*, 1954, **76**, 519; cf. Skraup and Beifuss, *Ber.*, 1927, **60**, 1070.

of phenol and (*via* its enol) acetaldehyde; but, as in the pyrolysis of 2-hydroxyethyl benzoate, the origin of water is less obvious. It cannot arise by intramolecular cyclodehydration to coumaran, or by intermolecular dehydration to 2 : 2′-diphenoxydiethyl ether, since neither of these substances was present in the pyrolysate, though both should be fairly thermostable. Direct intramolecular dehydration to water and phenyl vinyl ether remains as a possibility, though somewhat unexpected; the fact that only a trace of the ether was noted [11] may be accounted for by its secondary breakdown, discussed later.

Some of these conclusions conflict with the reported ready dehydration of 2-phenoxyethanol by chemical reagents, but it has not been possible to confirm these claims. For example, it has been stated [13] that it is cyclodehydrated to coumaran by treatment with phosphoric oxide or zinc chloride; several attempts to repeat this have failed, the former reagent yielding only tri-2-phenoxyethyl phosphate. Similarly, it could not be confirmed that 2-phenoxyethanol, treated with concentrated sulphuric acid, yields *o*-vinylphenol, as claimed by Smith and Niederl; [14] a similar negative result has recently been reported by Bader [15] and Knights and Cooper.[16]

2-*Phenoxyethyl Acetate* (VI).—Knights and Cooper [11,16] have found that pyrolysis of the acetate (VI) at *ca.* 600° yields acetic acid (33%), benzaldehyde (17%), phenol (11%), and a little vinyl acetate, but no phenyl vinyl ether or *o*-vinylphenol; *ca.* 30% of the material was lost as gases. The present work agrees with this in the main, but has shown in addition the formation of carbon monoxide and a little anisole, acetone, and phenyl vinyl ether. The whole complex breakdown is best interpreted by the following scheme of concurrent competitive scissions, which accounts for everything except the very unexpected formation of benzaldehyde :



The breakdown of the ether-ester (VI) predominantly as an ester (by the A^1 route, with a little acyl–oxygen scission, B^2), but also concurrently as an ether (by the $A^1{}_{OR}$ route), agrees with previous conclusions.[3] Phenoxyacetaldehyde itself was not found in the pyrolysate, but anisole and carbon monoxide, its predictable decarbonylation (C^1) products, were identified, as was acetone, a predictable scission product of vinyl acetate by the major R/C^1 sequence.[1] Benzaldehyde is the only product for which no obvious precursor suggests itself; clearly, its formation entails a step where the phenoxy-group is ruptured at the very stable phenyl–oxygen bond, and probably occurs by a radical reaction.

Phenyl Vinyl Ether (VII).—As a check on some of the foregoing views, phenyl vinyl ether was pyrolysed. Its thermal breakdown has been described previously, but the results are inconclusive and somewhat conflicting. Claisen [17] reported that it rearranges thermally, but Powell and Adams [18] reported that in a sealed tube at 260—280° there is

[13] Rindfusz, *J. Amer. Chem. Soc.*, 1919, **41**, 665; Rindfusz, Ginnings, and Harnack, *ibid.*, 1920, **42**, 157.
[14] Smith and Niederl, *ibid.*, 1931, **53**, 806.
[15] Bader, *ibid.*, 1955, **77**, 4155.
[16] Knights and Cooper, *Chem. and Ind.*, 1955, 1558.
[17] Claisen, G.P. 268,099/1913.
[18] Powell and Adams, *J. Amer. Chem. Soc.*, 1920, **42**, 646.

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slow decomposition to phenol, with no concurrent formation of acetylene, and a similar result was noted for *p*-tolyl vinyl ether. Lauer and Spielman [19] found that under similar conditions only a small amount of phenol was formed, together with diphenylacetal, $CHMe(OPh)_2$, and a tar with *M ca.* 800, but no acetylene: further, a mixture of the ether with phenol yielded more phenol than was present (free) in the mixed pyrolysand, with complete destruction of the ether. We have found that in a flow reaction vessel (*i.e.*, with a contact time very much less than in pyrolysis in a sealed tube) the ether (VII) breaks down primarily to phenol and acetylene at *ca.* 500°. There is a marked molar deficiency of the latter, and much tar is retained in the vessel: there is no evidence of any primary reaction other than this A^1_{OR} scission (*e.g.*, rearrangement to *o*-vinylphenol), or for formation of benzaldehyde (cf. pyrolysis of 2-phenoxyethyl acetate).

No clear-cut conclusion is possible, from the limited number of pyrolyses considered here, as to the factors promoting disproportionation. The *D* reaction undergone by substances (I) and (IV) suggests that the ester group common to both may be a promoting structure: and the failure of substances (V) and (VI) to disproportionate suggests that the phenoxy-group may be an inhibiting structure, even, in the latter example, to the extent ot overcoming the effect of the ester group also present. The formation of 1 : 2-diphenoxyethane by a side reaction when the ether (VII) is prepared by heating 2-bromoethyl phenyl ether with solid alkali (see Experimental) appears to constitute disproportionation of a compound containing a phenoxy-group (this by-product was not recorded by Chalmers,[20] although he noted a somewhat analogous side-reaction of alkyl 2-bromoethyl ethers), but this example is inconclusive because reactions other than disproportionation may formally be responsible for the diphenoxy-compound (*e.g.*, interaction of the starting material, in presence of alkali, with phenol produced by its own decomposition, or by that of phenyl vinyl ether).

Poly(ethylene Terephthalate) (II).—Application of the foregoing results to the pyrolysis of the polyester (II) leads to some interesting conclusions, subject to the usual proviso that caution is necessary in extrapolating results from vapour-phase to liquid-phase conditions. Since the initial concentration of 2-hydroxyethyl end-groups in the polyester (II) is low, disproportionation by their mutual intermolecular reaction will contribute only slightly to the initial pyrolytic changes. As the breakdown proceeds, however, and the molecules in the molten pyrolysand become smaller and more mobile, conditions will increasingly favour the continual interaction (disproportionation) of surviving 2-hydroxyethyl end-groups, just as they favour the continual ester-interchange (within the chain) described previously.[8] This *D* reaction will temporarily unite small molecules into longer chains, simultaneously producing water and assisting in the production of acetaldehyde and anhydride groupings, though the last two products are formed mainly by chain scission *via* the A^1/D mechanism.[6] At higher temperatures, A^1 scission of the 2-hydroxyethyl end-groups will compete more strongly with their *D* reaction, forming new carboxyl end-groups and at the same time providing a further route to acetaldehyde.

None of the various other models previously studied [1,3,8] as a guide to interpreting the thermal breakdown of poly(ethylene terephthalate) has yielded water on pyrolysis. The present work on model (I) suggests, therefore, that the small amount of water given by the polyester on pyrolysis [21] arises solely by way of 2-hydroxyethyl end-groups.

Experimental

Apparatus.—The arrangement of reaction vessel, furnace, traps, and receivers has been described.[1,3] Several vessels, of slightly different dimensions, were used; they were evacuated and thoroughly flushed with nitrogen before each run.

[19] Lauer and Spielman, *J. Amer. Chem. Soc.*, 1933, **55**, 1572.
[20] Chalmers, *Canad. J. Res.*, 1932, **7**, 464, 472.
[21] Pohl, *J. Amer. Chem. Soc.*, 1951, **73**, 5660.

Results.—Tables 1 and 2 summarise the general experimental results for 13 pyrolyses. The detailed examination of each liquid pyrolysate (*a*) is summarised below; the composition of gaseous pyrolysates (*b*) is reported on a nitrogen-free basis. The considerable overall losses recorded for several pyrolyses (*e.g.*, pyrolysis 10) are due to carbonisation and/or hold-up in the reaction vessel.

Analysis.—Aldehydes and ketones were characterised as their 2 : 4-dinitrophenylhydrazones (paper chromatography [22] and/or mixed m. p.); all other solids were identified by mixed m. p. Acid anhydrides were detected by the Davidson and Newman colour reaction,[23] and water by the anhydrous copper sulphate test. The normal chemical examination of fractions was in some cases supplemented by infrared spectrometry and vapour-phase chromatography.

TABLE 1. *Pyrolysis of 2-hydroxyethyl benzoate* (I), *2-chloroethyl benzoate* (IV), *and 2-phenoxyethanol* (V).

Pyrolysand	(I)	(I)	(IV)	(IV)	(IV)	(IV)	(V)
Pyrolysis no.	1	2	3	4	5	6	7
Temperature	375°	500°	400°	400°	450°	500°	500°
Feed-rate (g./min.)	0·34	0·54	0·43	0·48	0·51	0·57	0·39
Wt. pyrolysed (g.)	20·0	99·0	49·3	30·0	83·3	57·4	40·0
(*a*) Liquid pyrolysate (g.)	17·0	76·0	43·1	29·3	67·8	41·0	39·7
(*b*) Gaseous pyrolysate (l.)	Negl.	8·0	1·5	Negl.	2·0	Negl.	1·0
Composition (%) of (*b*) :							
CO	—	49·5	32·0	—	29·2	—	35·9
CO_2	—	1·8	23·3	—	55·4	—	Nil
CH_4	—	45·9	Nil	—	Nil	—	34·6
Unsat. hydrocarbons	—	2·8	44·7	—	15·4	—	29·5

— Not observed.

TABLE 2. *Pyrolysis of 2-phenoxyethyl acetate* (VI), *phenyl vinyl ether* (VII), *diethylene glycol* (III; X = OH), *2 : 2′-dichlorodiethyl ether* (III; X = Cl), *ethylene glycol* (VIII), *and 1 : 2-dichloroethane* (IX).

Pyrolysand	(VI)	(VI)	(VII)	(III : X = OH)	(III : X = Cl)	(VIII)	(IX)
Pyrolysis no.	8	9	10	11	12	13	14
Temperature	400°	500°	500°	375°	375°	375°	400°
Feed-rate (g./min.)	0·27	0·37	0·73	0·55	0·38	1·00	0·36
Wt. pyrolysed (g.)	65·4	96·0	22·0	50·0	50·0	25·0	10·3
(*a*) Liquid pyrolysate (g.)	63·3	89·0	10·0 *	46·0	34·0	23·2	7·6
(*b*) Gaseous pyrolysate (l.)	Negl.	14·0	1·0	Negl.	2·3	Negl.	†
Composition (%) of (*b*) :							
CO	—	34·9	—	—	—	—	—
CO_2	—	37·6	—	—	—	—	—
Unsat. hydrocarbons	—	27·5	‡	—	—	—	—

* Much carbonisation. ‡ Mainly acetylene.
† Contained hydrogen chloride (7·2% of theory). — Not observed.

2-Hydroxyethyl Benzoate (I).—*Preparation.* The pure benzoate (I), prepared (92%) by heating sodium benzoate with excess of ethylene chlorohydrin and a little diethylamine (140°; 4 hr.), had m. p. 37° (lit.,[24] 45°) and b. p. 146°/3 mm. (lit.,[3] b. p. 173°/21 mm.) (Found: C, 65·4; H, 6·1. Calc. for $C_9H_{10}O_3$: C, 65·1; H, 6·0%).

Pyrolysis 1. Acetaldehyde vapour was detected in the gaseous pyrolysate (*b*) by a 2 : 4-dinitrophenylhydrazine trap. Distillation of the liquid pyrolysate (*a*) yielded water (0·6 g.) and a residue which, when dissolved in ether and extracted with water and then with dilute alkali, yielded ethylene dibenzoate (major portion of pyrolysate), ethylene glycol (characterised as its dibenzoate), and only a trace of benzoic acid.

Pyrolysis 2. Distillation of (*a*) yielded acetaldehyde, 0·4 g. of a liquid, b. p. 80° (probably

[22] Burton, *Chem. and Ind.*, 1954, 576.
[23] Davidson and Newman, *J. Amer. Chem. Soc.*, 1952, **74**, 1515.
[24] Heim and Poe, *J. Org. Chem.*, 1944, **9**, 299; cf. also G.P. 245,532/1910.

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benzene), and 2·3 g. of water. Treatment of the residue with alkali removed benzoic acid (26·8 g.), leaving ethylene dibenzoate (24·1 g.) containing a little benzoic anhydride. Vinyl benzoate and acetophenone were not detected.

2-*Chloroethyl Benzoate* (IV).—*Preparation.* Prepared (85%) by heating benzoyl chloride (slight excess) with ethylene chlorohydrin (100°; 2 hr.), the pure benzoate had b. p. 152°/15 mm. (lit.,[25] b. p. 118—120°/2 mm.).

Pyrolysis 3. Hydrogen chloride was removed from (*b*) by a water trap (silver nitrate), and vinyl chloride (*ca.* 1·5 ml.) by the cold trap (infrared); a 2 : 4-dinitrophenylhydrazine trap showed only a trace of precipitate. Distillation of (*a*) yielded 12·9 g. of unchanged 2-chloroethyl benzoate, b. p. 160—180°/26 mm. (containing a little vinyl benzoate; infrared), and 17·5 g. of ethylene dibenzoate containing a trace of benzoic anhydride. Benzoic acid and 1 : 2-dichloroethane were not detected.

Pyrolysis 4. Hydrogen chloride and vinyl chloride were detected in (*b*) as before. Distillation of (*a*) yielded unchanged benzoate (IV) (24 g.), benzoic acid (3 g.), and a trace of ethylene dibenzoate.

Pyrolysis 5. Hydrogen chloride and vinyl chloride were detected in (*b*); a 2 : 3-dinitrophenylhydrazine trap showed a trace of precipitate. Distillation of (*a*) yielded unchanged benzoate (IV) (41 g.), benzoic acid (15 g.), and a liquid (*ca.* 1 g.), b. p. 215°/15 mm., which partly solidified, and which contained a little benzoic anhydride.

Pyrolysis 6. Hydrogen chloride and vinyl chloride were detected in (*b*); the cold trap contained a large condensate (*ca.* 25 ml.), in which vinyl chloride was detected by conversion into 1 : 2-dibromo-1-chloroethane, b. p. 163° (lit.,[9] b. p. 162·5—163°). Distillation of (*a*) yielded unchanged benzoate (IV) (12·3 g.), benzoic acid (23·0 g.), and a trace of liquid (*ca.* 0·1 g.), b. p. >280°, which partially solidified. Benzoic anhydride was present in (*a*).

2-*Phenoxyethanol* (V).—Pure material, from British Drug Houses Ltd., was used.

Pyrolysis 7. Acetaldehyde vapour was detected in (*b*) (2 : 4-dinitrophenylhydrazine trap). Distillation of (*a*) yielded water (2·7 g.); the residue, when dissolved in ether and washed with water, yielded no ethylene glycol; an alkali-soluble fraction (5 g.) was removed, which on acidification, extraction with ether, and distillation, yielded phenol (characterised as its benzoate) and unchanged 2-phenoxyethanol (V), b. p. 190—232° (infrared). No evidence could be found for the presence of phenyl vinyl ether (VII), diphenyl ether, diphenylacetal, or coumaran.

2-*Phenoxyethyl Acetate* (VI).—*Preparation.* Prepared (81%) by heating (V) with excess of acetic anhydride and a little pyridine (100°; 4 hr.), the pure acetate had b. p. 252—256° and n_D^{22} 1·504 (lit.,[26] b. p. 241—243°).

Pyrolysis 8. Acetaldehyde vapour (2 : 4-dinitrophenylhydrazine trap) was detected in (*b*), but no keten. Distillation of (*a*) yielded fractions (i)—(iv), b. p. 100—130°, 150—170°, *ca.* 180°, and 200° respectively, and a residue. Fraction (ii) contained anisole (characterised as 2 : 4-dinitroanisole) and on hydrolysis yielded acetaldehyde (indicating the presence of a vinyl ester and/or ether); fraction (iii) contained benzaldehyde, but gave a negative reaction (ferric chloride) for phenol; fraction (iv) was unchanged 2-phenoxyethyl acetate.

Pyrolysis 9. The cold trap contained some acetone. Liquid (*a*) was washed free from acetic acid, dried, and distilled, yielding fractions (i)—(vi), b. p. 145°, 150—160°, 170—180°, 180—200°, 200—220°, and 220—270° respectively, and a residue. Fraction (ii), treated with bromine–carbon tetrachloride, yielded 1 : 2-dibromoethyl phenyl ether (16 g.), b. p. 120°/6 mm., n_D^{δ} 1·585 (lit.,[27] b. p. 140—145°/18 mm., n_D^{20} 1·5845), and was hence largely starting material; fraction (iv) contained carbon monoxide and dioxide, methane, ethylene, and acetylene (infrared).

Phenyl Vinyl Ether (VII).—*Preparation.* 2-Bromoethyl phenyl ether (400 g.) was refluxed (5 hr.) with solid sodium hydroxide (400 g.). Distillation yielded a liquid, b. p. *ca.* 100° (probably an azeotrope: separated into two layers), followed by 120 g. (56%) of 1 : 2-diphenoxyethane, b. p. 292—295°/6 mm., m. p. 98° (from ethanol), mixed m. p. 98°. The low-boiling fraction, on extraction with ether and distillation, yielded crude phenyl vinyl ether; refractionation yielded 22 g. (18%) of pure ether (VII), b. p. 155—158° (lit.,[18, 19] b. p. 155—156°).

Pyrolysis 10. Treatment with alkali divided (*a*) into phenol (6 g.; characterised as its

[25] Kirner, *J. Amer. Chem. Soc.*, 1926, **48**, 2745.
[26] Roithner, *Monatsh.*, 1894, **15**, 675.
[27] McElvain and Fajardo-Pinzón, *J. Amer. Chem. Soc.*, 1945, **67**, 650.

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benzoate; vapour-phase chromatography demonstrated the absence of *o*-cresol and *o*-vinylphenol) and an unidentified alkali-insoluble fraction (4 g.; b. p. 120—135°) which decolorised bromine–carbon tetrachloride and gave no 2 : 4-dinitrophenylhydrazone. The gaseous pyrolysate (*b*) was mainly acetylene (infrared).

Diethylene Glycol (III; X = OH).—Purified material, from British Drug Houses Ltd., was used.

Pyrolysis 11. Distillation of (*a*) yielded water (<1 g.; anhydrous copper sulphate test). Acetaldehyde was readily detected (chromatography of 2 : 4-dinitrophenylhydrazone).

2 : 2′-*Dichlorodiethyl Ether* (III; X = Cl).—Purified material, from British Drug Houses Ltd., was used.

Pyrolysis 12. The gaseous pyrolysate contained hydrogen chloride (water trap; silver nitrate) and acetaldehyde (2 : 4-dinitrophenylhydrazine trap). The cold trap collected *ca.* 1·8 g. of volatile liquid, containing vinyl chloride (infrared) and acetaldehyde.

Ethylene Glycol.—Purified material, from British Drug Houses Ltd., was used. Its water content was 0·26% (Karl Fischer method).

Pyrolysis 13. The liquid (*a*) was essentially unchanged ethylene glycol, containing no diethylene glycol (infrared), but with a water content of 2·10% (*i.e.*, about eight times the original value). No measurable amount of acetaldehyde was detected.

1 : 2-*Dichloroethane*.—Purified material, from British Drug Houses Ltd., was used.

Pyrolysis 14. The extent of decomposition was determined by passing the gaseous pyrolysate (*b*) through a water trap and titrating the dissolved hydrogen chloride (7·2% of theory).

Attempted Dehydrations (*Non-pyrolytic*) *of* 2-*Phenoxyethanol* (V).—The following reagents were applied:

(i) *Phosphoric oxide*. 2-Phenoxyethanol (excess) was slowly added to a suspension of phosphoric oxide in benzene; after refluxing (2 hr.), removal of solvent yielded tri-2-phenoxyethyl phosphate, m. p. 142° (from acetone), mixed m. p. 140°. Distillation of 2-phenoxyethanol over phosphoric oxide led to profound decomposition.

(ii) *Acetic acid and anhydride*. Treatment of 2-phenoxyethanol with glacial acetic acid and fused zinc chloride, or with acetic anhydride and pyridine, led only to formation of its acetate (VI).

(iii) *Sulphuric acid*. Treatment of 2-phenoxyethanol with cold concentrated or fuming sulphuric acid (7 days) caused little or no change; treatment at 100° (4 hr.) yielded an unidentified white solid, insoluble in ether but extremely soluble in water, which was certainly not *o*-vinylphenol (cf. Smith and Niederl [14]).

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498. *Studies in Pyrolysis. Part XI.* Competitive Routes in the Pyrolysis of Esters: Phenyl Acrylate and Phenyl α-Methylacrylate.*

By H. M. Mackinnon and P. D. Ritchie.

Pyrolysis of phenyl acrylate (or α-methylacrylate) in the vapour phase occurs at *ca.* 550° mainly by two competitive routes: (i) intra-acyl scission to acetylene (or methylacetylene) and phenyl formate, with secondary decarbonylation of the latter to phenol and carbon monoxide, and (ii) decarboxylation to styrene (or α-methylstyrene) and carbon dioxide. Reaction (i), which predominates, is suppressed by the addition of quinol to the pyrolysand; reaction (ii) is not. A tentative free-radical mechanism for reaction (i) is suggested. Minor competitive primary and secondary reactions are described.

Although thermal decarboxylation of many carboxylic acids is well established,[1] decarboxylation of their esters was for long represented by only very few examples,[2,3] such as the following:[2]

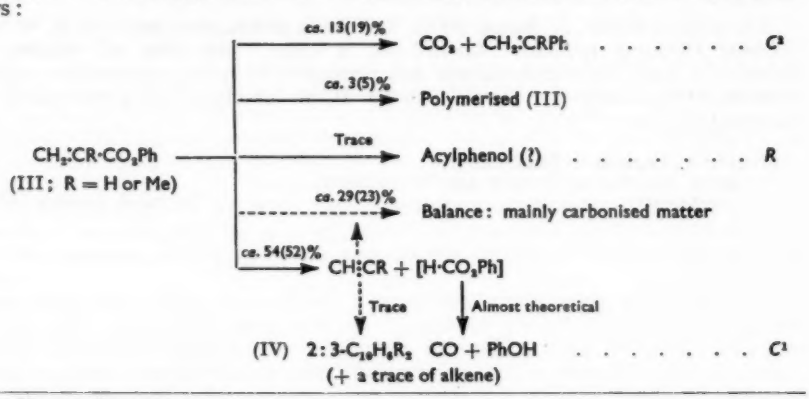
$$\begin{matrix}\text{CH·CO}_2\text{Ph}\\ \|\\ \text{CH·CO}_2\text{Ph}\\ \text{(cis or trans)}\end{matrix} \xrightarrow[C^1]{-CO_2} \text{Ph·CH:CH·CO}_2\text{Ph} \xrightarrow[C^1]{-CO_2} \underset{\text{(trans)}}{\text{Ph·CH:CH·Ph}}$$

Recently, however, decarboxylation (C^2) has been observed[4] as a competitive route in the complex pyrolysis of various vinyl carboxylates (I), and also[5] of αα-dicyanobenzyl benzoate (II):

$$\text{(I)}\quad \text{R·CO}_2\text{·CH:CH}_2 \longrightarrow \text{CO}_2 + \text{CH}_2\text{:CHR} \quad \ldots\ldots\ldots\ C^2$$

$$\text{(II)}\quad \text{Ph·CO}_2\text{·CPh(CN)}_2 \longrightarrow \text{CO}_2 + \text{CPh}_2\text{(CN)}_2 \quad \ldots\ldots\ldots\ C^2$$

It now seems probable, therefore, that the C^2 reaction is more important in ester pyrolysis than previously appeared, and deserves further study. A comparison of the pyrolysis[4] of vinyl benzoate (I; R = Ph) with that of its structural isomer, phenyl acrylate, suggested itself as a first step in studying the factors which dictate that an ester shall undergo thermal decarboxylation. It has now been found that phenyl acrylate (III; R = H) and phenyl α-methylacrylate (III; R = Me), both of which are remarkably stable up to *ca.* 500°, break down at *ca.* 550° to the extent of *ca.* 50% in the flow system employed (Table 1, runs 1—4) by a series of competitive reactions (including decarboxylation), best represented as follows:



* Part X, preceding paper.

[1] Hurd, "The Pyrolysis of Carbon Compounds," Chemical Catalog Co., New York, 1929, Chap. 13.
[2] Anschütz, *Ber.*, 1885, **18**, 1945; Anschütz and Wirtz, *Ber.*, 1885, **18**, 1947; Bischoff and von Hedenström, *Ber.*, 1902, **35**, 4084; Anschütz, *Ber.*, 1927, **60**, 1320.
[3] Roberts and Bowden, *Rec. Trav. chim.*, 1930, **49**, 665.
[4] Allan, Forman, and Ritchie, *J.*, 1955, 2717.
[5] Bennett, Jones, and Ritchie, *J.*, 1956, 2628.

The figures above each horizontal arrow represent the approximate weight-contribution of each competing route to the overall pyrolysate from the acrylate and (in parentheses) the α-methylacrylate; within reasonable limits of experimental error, the molar ratio of the various routes is the same for each pyrolysand. The broken arrows indicate the most probable source of the observed tar, and of the naphthalenes (IV; R = H or Me).

Discussion

Intra-acyl Scission.—The major primary breakdown route shown above, leading to an alkyne and phenyl formate, is of a novel type corresponding to scission within the $CH_2{:}CR{\cdot}CO{\cdot}$ grouping, which may thus be appropriately designated *intra-acyl scission.* This observation confirms Skraup and Nieten's report [6] that phenyl acrylate breaks down to phenol (64%), carbon monoxide, and acetylene at *ca.* 300—320° (sealed tube; 64 hr.), though these workers did not record decarboxylation or any other competing reaction. Since phenyl acetate (which like the acrylate and α-methylacrylate is very thermostable) breaks down [7] at *ca.* 600° to keten and phenol by acyl–oxygen (B^1) scission, it might be expected that phenyl acrylate would also break down primarily in a similar way, thus:

$$CH_2{:}CH{\cdot}CO{:}OPh \xrightarrow{?} [CH_2{:}C{:}CO] + PhOH \quad \ldots\ldots\ldots \quad B^1$$

Although the keten (methyleneketen) predicted on this basis does not appear to be known, it should be highly unstable, and might be expected to break down by a secondary decarbonylation (C^1), thus accounting for the other two products accompanying phenol in the pyrolysate:

$$[CH_2{:}C{:}CO] \xrightarrow{?} CH{\vdots}CH + CO \quad \ldots\ldots\ldots\ldots \quad C^1$$

While the above sequence might formally occur for the acrylate (III; R = H), it is precluded for the α-methylacrylate (III; R = Me) by replacement of the α-hydrogen atom **H** by the less mobile methyl group, and cannot explain the formation of phenol (with no evidence for any formation of anisole) on pyrolysis of the latter ester (Table 1, runs 3—4). The evidence, therefore, favours the alternative explanation of a primary competitive scission to an alkyne ($CH{\vdots}CR$) and phenyl formate. The latter ester is known [8] to break down to carbon monoxide and phenol on distillation; and it is now found (Table 1, run 5) that this decarbonylation is almost theoretical in the vapour phase at *ca.* 550°. There is no evidence for formation of benzene by competitive decarboxylation (in marked contrast to the thermal breakdown [3] of triphenylmethyl formate by the C^2, but not the C^1, reaction), and not more than a trace of phenyl formate survives in the pyrolysate.

Both acrylate and α-methylacrylate yield a small trace of phenyl formate, thus confirming the above mode of intra-acyl scission; but the accompanying alkyne ($CH{\vdots}CR$) is much less than equivalent in amount to the observed carbon monoxide and phenol (Table 1, runs 1—4). This deficiency can be attributed to partial secondary destruction of the alkyne; for example, the observed traces of a naphthalene (IV; R = H or Me) are most probably due to pyrolysis of the alkyne, on the classical lines recorded by Berthelot,[9] though this is of secondary importance to the formation of much carbonised matter and tar. (It has similarly been noted [10] that pyrolysis of phenyl vinyl ether at *ca.* 500°, which yields acetylene and phenol in a molar ratio much less than unity, also leads to heavy carbonisation.) In the present pyrolyses, tar formation from phenyl acrylate can be

[6] Skraup and Nieten, *Ber.*, 1924, **57**, 1294.
[7] Ritchie, unpublished observation, 1934,; Hurd and Blunck, *J. Amer. Chem. Soc.*, 1938, **60**, 2419.
[8] Adickes, Brunnert, and Lücker, *J. prakt. Chem.*, 1931, **130**, 163.
[9] Berthelot, *Ann. Chim. Phys.*, 1866, [4], **9**, 445.
[10] Iengar and Ritchie, preceding paper.

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correlated roughly with the extent of intra-acyl scission (cf. Table 2); nevertheless, there must be some tar-producing reaction other than mere secondary breakdown of the alkyne, since there is more carbonised matter than can be accounted for on this basis. This is indicated in the foregoing overall reaction-scheme for the esters (III).

The effect of various inhibitors on the competitive pyrolyses has been studied for the acrylate (III; R = H); and it is found that although the C^2 reaction is not consistently and significantly affected, the intra-acyl scission is completely suppressed by addition of 1% of quinol to the pyrolysand (Table 2). This suggests that the latter breakdown is free-radical in character; and the following sequence is tentatively suggested:

Initiation

(i) $CH_2{:}CR{\cdot}CO_2Ph \longrightarrow CH_2{:}CR\cdot + \cdot CO_2Ph$

Propagation

(ii) $CH_2{:}CR\cdot + CH_2{:}CR{\cdot}CO_2Ph \longrightarrow \cdot CH{:}CR{\cdot}CO_2Ph + CH_2{:}CHR$

(iii) $\cdot CH{:}CR{\cdot}CO_2Ph \longrightarrow CH{:}CR + \cdot CO_2Ph$

(iv) $\cdot CO_2Ph + CH_2{:}CR{\cdot}CO_2Ph \longrightarrow H{\cdot}CO_2Ph + \cdot CH{:}CR{\cdot}CO_2Ph$ (etc.)

$\downarrow$

$CO + PhOH$

It is possible that the following stages, (v) and (vi), may compete with (ii), (iii), and (iv); but they cannot represent the only breakdown of the phenoxycarbonyl radicals $\cdot CO_2Ph$, since they offer no explanation for the observed formation of phenyl formate:

(v) $\cdot CO_2Ph \longrightarrow CO + \cdot OPh$

(vi) $\cdot OPh + CH_2{:}CR{\cdot}CO_2Ph \longrightarrow PhOH + \cdot CH{:}CR{\cdot}CO_2Ph$ (etc.)

Decarboxylation (C^2).—The present results clarify and reconcile certain apparently conflicting earlier reports. Filachione *et al.*[11, 12] showed that various aryl α-acetoxypropionates (V), which on pyrolysis yield mainly the predictable A^1 scission products (acetic acid and aryl acrylate), also yield a small amount of a styrene; this result can now be convincingly interpreted by the following reaction sequence:

(V) $AcO{\cdot}CHMe{\cdot}CO_2Ar \longrightarrow AcOH + CH_2{:}CH{\cdot}CO_2Ar$ . . . . . A^1

$CH_2{:}CH{\cdot}CO_2Ar \longrightarrow CO_2 + CH_2{:}CHAr$ . . . . . C^2

(Ar = phenyl [11] or *p*-*tert*.-butylphenyl [12])

In addition, however, it was noted [12] that where Ar = *m*-tolyl the pyrolysate (again consisting mainly of the A^1 products) contains a little *m*-cresol. This is now explicable on the basis of a competitive secondary intra-acyl scission of *m*-tolyl acrylate; it accords with the present results, and with Skraup and Nieten's observations,[6] although the latter workers had recorded nothing which could explain the formation of a styrene from the ester (V).

Formally, the C^2 reaction requires scission of the ester molecule at two points, with combination of the two terminal fragments (alkenyl and aryl); and it is difficult to visualise this as occurring except *via* a free-radical mechanism. Nevertheless, none of the arbitrarily chosen inhibitors listed in Table 2 has any significant effect on the extent of the C^2 reaction, and for the present it is preferred not to suggest any detailed mechanism for the decarboxylation.

Other Competitive Routes.—Formation of a little polymerised acrylate (III) calls for no special comment; and the observed traces of alkene in the gaseous pyrolysates may be

[11] Filachione, Lengel, and Fisher, *J. Amer. Chem. Soc.*, **1944**, **66**, 494.
[12] Filachione, Lengel, and Ratchford, *ibid.*, 1950, **72**, 839.

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accounted for by the tentative free-radical mechanism outlined. Separate pyrolyses of phenyl formate, styrene, and α-methylstyrene under the same conditions (Table 1, runs 5—7) show that secondary breakdown of these primary products is not responsible *per se* for any of the other minor components of the pyrolysate, or for tar formation.

Skraup and Beng [13] have recorded the thermal Fries-type rearrangement of phenyl ββ-dimethylacrylate to *o*-ββ-dimethylacryloylphenol, which suggests that the acrylate and α-methylacrylate might rearrange analogously to the corresponding *o*-acryloyl- or *o*-α-methylacryloyl-phenol. Some evidence for this has been found, though it is not conclusive. A very minor fraction was obtained (Table 1, runs 1—4) which in each case showed both ketonic and phenolic properties: neither this nor its derivatives could be isolated rigorously pure, but it yielded a trace of a crude 2 : 4-dinitrophenylhydrazone which in its purest form gave (like the parent fraction itself) the colour reactions of a phenol.

Filachione *et al.*[12] found that the pyrolysate from the ester (V; Ar = *m*-tolyl or *p*-chlorophenyl) contained a little diacetyl. This α-diketone has not been found in the pyrolysate from phenyl acrylate (indeed, this was hardly to be expected), and the conclusion is that it must arise *via* a competitive primary route in the pyrolysis of the ester (V) itself. This view is confirmed by the isolation [14] of an α-diketone in the pyrolysate from several other α-substituted esters, an observation which will be more fully described in a later paper.

Experimental

Apparatus and Procedure.—These have been described previously.[4] The free unpacked space in the reaction vessel was 220 ml., except in run 12 (Table 2). Before each run, carbonised deposits from the previous run were thoroughly removed by heating the vessel to 500° in a current of air, in order to minimise catalytic effects of the type described by Bailey *et al.*[15]

Preparation of Pyrolysands.—Phenyl acrylate. Acryloyl chloride, prepared [16] from acrylic acid and benzoyl chloride, was treated with phenol in the presence of a little quinol. The crude phenyl ester was fractionally distilled over copper turnings immediately before use (yield *ca.* 65%, b. p. 87—94°/12 mm., n_D^{20} 1·523; Filachione *et al.*,[11] b. p. 87—94°/12 mm., n_D^{20} 1·520).

Phenyl α-methylacrylate. This was prepared on the same lines as the acrylate (yield *ca.* 60%, b. p. 98—102°/12 mm., n_D^{20} 1·515; Filachione *et al.*,[12] b. p. 47—50°/0·2 mm., n_D^{20} 1·5147; Du Pont,[17] b. p. 83—84°/4 mm.).

Phenyl formate. This was prepared as described by Adickes *et al.*,[8] intensive fractionation under reduced pressure leading to pure material (yield *ca.* 10%, b. p. 82—83°/15 mm.) showing negative colour tests for free phenol.

Styrene and α-methylstyrene. Commercial styrene (British Drug Houses Ltd.) and α-methylstyrene (L. Light & Co. Ltd.) were carefully fractionated, and products with b. p. 146° and b. p. 162° respectively were used for pyrolysis.

Results.—Table 1 summarises the overall conditions and results for 7 runs; all gas analyses (*b*) are reported on a nitrogen-free basis. A satisfactory reproducibility is indicated by comparison of runs 1 and 2, and of runs 3 and 4; but the weights of the various fractions are subject to an estimated error of ±10% owing to manipulative difficulties in purifying small quantities of pyrolysate, and a high degree of accuracy is therefore not claimed for the figures in Tables 1 and 2. In run 12, copper exhibited a promoting rather than an inhibiting effect on the overall pyrolysis; and after this run the walls of the Pyrex-glass reaction vessel were strongly stained with a uniform clear copper-brown colour, which could not be removed by heating at 500° in a current of air or by treatment with mineral acid.

Analysis.—The liquid pyrolysates (*a*) were fractionally distilled, to recover and determine unchanged pyrolysand. The remaining major components were characterised as follows,

[13] Skraup and Beng, *Ber.*, 1927, **60**, 942.
[14] Jones and Ritchie, unpublished observation.
[15] Bailey and Rosenberg, *J. Amer. Chem. Soc.*, 1955, **77**, 73; Bailey and King, *ibid.*, p. 75; Bailey, Hewitt, and King, *ibid.*, p. 357.
[16] Stempel, Cross, and Mariella, *ibid.*, 1950, **72**, 2299; Brown, *ibid.*, 1938, **60**, 1325.
[17] Du Pont, *Ind. Eng. Chem.*, 1936, **28**, 1160.

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all solid products (or derivatives) being identified by mixed m. p.: (i) Phenol as benzoate; (ii) styrene (b. p. 146°) as 1′ : 2′-dibromoethylbenzene; (iii) α-methylstyrene (b. p. 162°) as 1′ : 2′-dibromo-1′-methylethylbenzene, b. p. 115—125°/8 mm. (Grignard,[18] b. p. 115°/8 mm.), and by oxidation (permanganate) to acetophenone (2 : 4-dinitrophenylhydrazone); (iv) phenyl

TABLE 1. *Pyrolysis of esters* (III; R = H *or* Me) *and related substances* (550°).

Pyrolysand	(III; R = H)		(III; R = Me)		Phenyl formate	Styrene	α-Methyl-styrene
Run no.	1	2	3	4	5	6	7
Feed-rate (g./min.)	0·33	0·38	0·28	0·30	0·36	0·36	0·26
Contact time (sec.)	88	76	113	106	66	57	89
Wt. pyrolysed (g.)	69	60	43	48	52	77	46
(*a*) Liquid pyrolysate (g.)	66	55	38	42	39	76	45
Pyrolysand unchanged (%)	48	49	49	54	Trace	*ca.* 99	*ca.* 99
(*b*) Gaseous pyrolysate (l.)	3·2	2·2	3·2	3·5	10·4	Negl.	Negl.
Composition (%) of (*b*):							
CO	62·0	58·8	55·2	50·1	99·5	—	—
CO_2	23·2	23·2	38·1	40·9	Trace	—	—
Unsat. hydrocarbons	14·8	18·0	6·7	9·0	Nil	—	—
Pyrolysand destroyed [g. (mol.)]	36(0·24)	31(0·21)	22(0·14)	22(0·14)	52(0·42)	Trace	Trace
Intra-acyl scission products [g. (mol.)]:							
PhOH	13·1(0·14)	10·0(0·11)	6·8(0·07)	6·0(0·07)	39·0(0·42)	—	—
CO	2·3(0·08)	1·6(0·06)	2·8(0·08)	2·1(0·08)	12·3(0·44)	—	—
$CH_2{:}CR$	0·5(0·02)	0·4(0·02)	0·4(0·02)	0·5(0·02)	—	—	—
Phenyl formate	Trace	Trace	Trace	Trace	Trace	—	—
Decarboxylation products [g. (mol.)]:							
$CH_2{:}CRPh$	2·9(0·03)	2·2(0·02)	2·6(0·02)	3·3(0·03)	—	—	—
CO_2	1·4(0·03)	1·0(0·02)	2·4(0·05)	2·7(0·06)	—	—	—
Other products (g.):							
Carbonised material	14·5	13·9	4·6	5·2	—	—	—
(IV; R = H or Me)	Trace	Trace	Trace	Trace	—	—	—
Acylphenol (?)	Trace	Trace	Trace	Trace	—	—	—
Alkene	Trace	Trace	Trace	Trace	—	—	—
Polymer	0·9	1·0	1·4	1·6	—	Trace	Trace

TABLE 2. *Effect of free-radical inhibitors on pyrolysis of phenyl acrylate* (550°).

Inhibitor	None	Quinol	Phenanthra-quinone	4-*tert.*-Butylcatechol	Benzo-quinone	Copper
Run no.	1—2 *	8 †	9 †	10 †	11 †	12 ‡
Feed-rate (g./min.)	0·36	0·35	0·34	0·30	0·30	0·32
Contact time (sec.)	82	83	85	97	97	110
Gaseous pyrolysate (l./g. of pyrolysand)	0·04	0·02	0·07	0·09	0·11	0·17
Ester unchanged (%)	48·5	91	74	63	33	22
Intra-acyl scission (%)	28	Nil	9	15	28	29
Decarboxylation (%)	7	7	3	9	11	10
Polymerisation (%)	2	Nil	6	5	6	6
Carbonisation (%)	15	2	8	8	22	33

* Figures represent average of the concordant runs 1 and 2 (Table 1).
† Inhibitor (1%) dissolved in pyrolysand.
‡ Reaction vessel packed with copper turnings instead of Pyrex-glass rings; free unpacked space 270 ml.

formate (b. p. 173° decomp.) by infrared absorption, and by preparation of formanilide from its hydrolysis product; (v) naphthalene (m. p. 78°) by mixed m. p.; (vi) 2 : 3-dimethylnaphthalene (m. p. 100°) by mixed m. p. [Found: C, 92·8; H, 7·8; *M* (cryoscopic in benzene), 150. Calc. for $C_{12}H_{12}$: C, 92·3; H, 7·7%; *M*, 156]; (vii) acetylene by infrared absorption; (viii) methylacetylene by infrared absorption (no evidence for any isomerisation to allene).

Distillation of (*a*), runs 1 and 2, gave a small oily fraction *A*, b. p. *ca.* 118°/10 mm.: distillation of (*a*), runs 3 and 4, gave a similar small fraction *B*, b. p. *ca.* 130°/10 mm. *A* and *B* both

[18] Grignard, *Compt. rend.*, 1902, **134**, 845.

gave the colour reaction (ferric chloride) of a phenol and both yielded a trace of a 2 : 4-dinitrophenylhydrazone (giving the phenol colour reaction) which could not be obtained rigorously pure. The 2 : 4-dinitrophenylhydrazones had m. p. 239—240° (Found : N, 21·6. Calc. for $C_{15}H_{12}O_5N_4$: N, 17·1%) and m. p. 254° (Found : C, 54·0; H, 3·8. Calc. for $C_{16}H_{14}O_5N_4$: C, 56·1; H, 4·1%), respectively.

The authors thank Mr. R. H. Wiseman and Mr. I. S. Young for assistance in the preliminary stages, Dr. W. I. Bengough for helpful discussions, and Imperial Chemical Industries Limited for a gift of materials.

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499. *The Blue Perchromic Acid.*

By ABRAHAM GLASNER and MENACHEM STEINBERG.

The composition of the blue perchromic acid has been elucidated in several ways. Photometric measurements of ethyl acetate extracts show that in aqueous solutions it is formed from two molecules of hydrogen peroxide and one molecule of chromic acid. The determination of the residual sexivalent chromium in the aqueous solutions, after extraction, confirms the ratio $H_2O_2/CrO_3 = 2$.

75% Acetone–water and 75% dioxan–water (v/v) * solutions were examined by Job's method.[1] In both media the maxima of the Job curves correspond to the ratio $H_2O_2/CrO_3 = 2$ if equimolar solutions of hydrogen peroxide and sodium chromate are employed, but on using an equimolar solution of potassium dichromate the ratio $H_2O_2/K_2Cr_2O_7 = 3$ is obtained. The discrepancy is attributed to the slow formation and decomposition of the per-compound causing a small shift in the position of the maxima of the Job curves. This shift is more exaggerated in the dichromate variations. Hence, it is concluded that Schwarz and Giese's [2] formula CrO_5 for the blue perchromic acid is correct.

ON evidence from the optical density of *ca.* 76% alcohol–water solutions, it has been concluded [3] that the blue perchromic acid is formed from hydrogen peroxide and chromic acid in the ratio 3 : 2. It was, therefore, given the formula $HCrO_5$, partial reduction of the chromium to the quinquevalent state being assumed. This concept was in accord with Riesenfeld's results.[4] It also offered an explanation of the intense colour, instability, and spontaneous decomposition of the per-acid to one containing tervalent chromium. On the other hand, Schwarz and Giese's results,[2] and some properties of the per-compound, could not be explained on the basis of the given formula (for literature see refs. 1—4). More experimental evidence on the composition of this unusual per-compound has therefore been sought.

A new experimental approach has been opened by the findings that the blue perchromate ion is quite stable in ethyl acetate solutions [5] and that chromium in either minerals or alloys can be determined quantitatively by measuring the optical density of the ethyl acetate extract of the blue per-acid formed in aqueous solutions.[6] Besides,

* 75% Acetone–water, *e.g.*, in this paper refers to a solution made by diluting 75 parts by volume of acetone to 100 parts by volume.

[1] Vosburgh and Cooper, *J. Amer. Chem. Soc.*, 1941, **63**, 437.
[2] Schwarz and Giese, *Ber.*, 1932, **65**, 871; 1933, **66**, 310; 1936, **69**, 575.
[3] Glasner, *J.*, 1950, 2795, see also Bobtelsky, Glasner, and Bobtelsky-Chaikin, *J. Amer. Chem. Soc.*, 1945, **67**, 966.
[4] Riesenfeld *et al.*, *Ber.*, 1905, **38**, 1885, 3380, 3578, 4068; 1908, **41**, 2826, 3536, 3941; 1914, **47**, 584.
[5] Brookshier and Freund, *Analyt. Chem.*, 1951, **23**, 1110.
[6] Glasner and Steinberg, *ibid.*, 1955, **27**, 2008.

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Job's method of "continuous variations" has been employed in the investigation of cooled acetone–water and dioxan–water solutions.

Our results indicate a ratio $H_2O_2/CrO_3 = 2$, and Glasner's previous conclusion [2] should be revised accordingly.

Experimental and Results

Materials.—Stock solutions of CrO_3, $K_2Cr_2O_7$, and Na_2CrO_4 of analytical grade (Baker's Analysed, or May and Baker's) were diluted as required. The concentration of the dichromate solution was determined by accurate weighing of the powdered salt dried at 160°, and the concentration of the other chromium solutions was standardized potentiometrically against it, a solution of Mohr's salt being used as titrant.

Hydrogen peroxide (May and Baker, 100 vol.) was diluted as required, and its concentration determined by use of a permanganate solution standardized with the primary dichromate solution.

Dilute sulphuric, hydrochloric, and perchloric acid were prepared from reagents of analytical quality. Ethyl acetate, acetone, and dioxan were Baker's C.P., May and Baker's, and "AnalaR." The ethyl acetate from the three firms was equally good, and was occasionally redistilled for repeated use. Only freshly opened bottles of dioxan were usable, because the presence of peroxides had an understandably disturbing effect.

Apparatus.—Measurements were made with Unicam (Model S.P. 350), Beckman DU, and Beckman B spectrophotometers, as convenient. The maximum on the absorption spectra of ethyl acetate extracts [6] as well as that of the mixed solvents occurred at 580 mμ, and all results recorded were obtained at this wavelength.

Extractions.—Solutions of the various reagents were measured by microburettes into 50-ml. flasks, cooled in ice–water. Hydrogen peroxide was always added last with vigorous mixing for 30 sec. The solutions were allowed 120 sec. to separate, and the organic solvent was transferred by pipette into the photometric cuvette, to be measured soon. The periods indicated were found best by experiment and were strictly adhered to; they allowed sufficient time for complete reaction while anticipating the decomposition of the perchromic acid.

Ethyl acetate extracted the blue perchromic acid formed in acid solutions, but not the violet alkali perchromate formed in dichromate solutions to which no mineral acid had been added.

Composition of the Blue Perchromic Acid in Ethyl Acetate Extracts.—Several series of solutions were prepared in which the concentration of either chromic acid or hydrogen peroxide was kept constant, whilst the concentration of the other reagent was increased stepwise. The optical densities of the ethyl acetate extracts increased linearly to a maximum that slightly fluctuated on further additions of the varying reagent. A plot of the optical densities gave, therefore, two straight lines intersecting at a point that indicates the ratio of hydrogen peroxide to chromium in the per-compound.

In Table 1 the ratios H_2O_2/CrO_3 obtained from such series of measurements are summarized. The solutions were mostly acidified by hydrochloric acid, though extractions with other mineral acids were quite as good.[8] Clearly, the ratios H_2O_2/CrO_3 approximate to 2, with a tendency to higher values in the series with fixed concentrations of chromium, and to lower values in the series with fixed concentrations of hydrogen peroxide, *i.e.*, the ratios deviate from 2 to the benefit of the varying reactant in a series. This is because the extraction of the perchromic acid is more favoured in the presence of an excess of any one of the reactants, and consequently, the inclination of the rising straight line is always somewhat less, and the point of intersection at somewhat larger concentrations of the reagent being varied, than the theoretical value.

Analysis of the Residual Chromium in the Aqueous Solution, after Extraction.—In a series of solutions the concentration of the chromate left in the aqueous solution after extraction was determined by the diphenylcarbazide method.[9] Each solution contained initially 1 ml. of M/75-$K_2Cr_2O_7$ and x ml. of 2M/75-H_2O_2. In Table 2 are shown the analytical results, together

[7] Job, *Ann. Chim.* (*France*), 1928, **9**, 113; 1936, **6**, 97; cf. Martell and Calvin, "Chemistry of the Metal Chelate Compounds," Prentice-Hall, New York, 1953, p. 29.

[8] Troitskii, *Zhur. Analit. Khim.*, 1954, **9**, 51.

[9] Sandell, "Colorimetric Determination of Traces of Metals," Interscience, New York, 1944, pp. 191—195.

TABLE 1. *Molar ratios of hydrogen peroxide to chromic acid in ethyl acetate extract.*

Total vol. of aqueous soln. (ml.)	Reagent not varied (ml.; M) *	Final concn. of HCl in aqueous layer (10^{-2}M)	Pyridine added †	Ratio H_2O_2/CrO_3
	CrO_3			
3	1·0; 0·00906	0·8	—	2·05
5	1·0; 0·00906	1·0	—	2·13
5	1·0; 0·00906	1·0	+	1·98
5	1·0; 0·00906	2·0	—	2·17
5	0·5; 0·00466	3·0	—	2·12
10	1·0; 0·00906	1·0	+	2·50
	$K_2Cr_2O_7$			
5	1·0; 0·005123	1·0	—	2·18
5	0·5 0·005123	2·0	—	2·18
	I_2O_2			
5	1·0; 0·01859	1·0	—	1·99
5	1·0; 0·01927	1·0	+	1·82
10	2·0; 0·00887	1·0	+	1·99
10	1·0; 0·01030	1·0	+	1·75
10	1·5; 0·01269	0·75	—	1·94

* *I.e.*, Quantity (ml.) of a solution of molarity M taken. † 0·5 ml. of a 0·04M-soln. in water.

TABLE 2. *Hydrogen peroxide/chromic acid ratio by the determination of the residual chromate.*

x	0·5	1·0	1·5	2·0	2·5	3·0
$K_2Cr_2O_7$ in residue (ml. of M/75 soln.)	0·77	0·52	0·247	0·007	0·00	0·00
H_2O_2/CrO_3 in extract	2·17	2·08	1·99	2·01	—	—

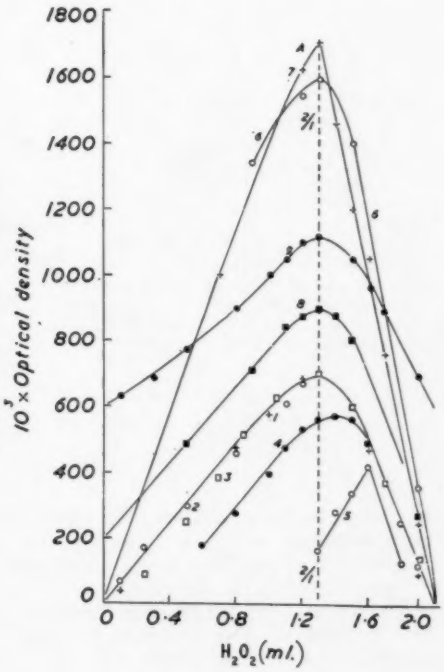


FIG. 1. *Job curves of 75% acetone–water mixtures.*

Curves 1—5: Variations with M/50 solutions of Na_2CrO_4 and H_2O_2, acidified by $HClO_4$; final concn. of acid: 1, 0·05M; 2, 0·01M; 3, 0·005M; 4, 0·0038M; 5, 0·0019M.

Curve 6: Variations with M/25 solutions of CrO_3 and H_2O_2, with final concn. of $HClO_4$ = 0·01M.

Curve 7(A): Variations with M/50-$K_2Cr_2O_7$ and M/25-H_2O_2, with final concn. of $HClO_4$ = 0·02M.

Curve 8: Variations with M/50 solns. of Na_2CrO_4 and H_2O_2, with final concn. of H_2SO_4 = 0·01N (reduce scale on ordinate by 200 units).

Curve 9: Variations with M/75 solns. of Na_2CrO_4 and H_2O_2, with final concn. of $HClO_4$ = 0·01M (reduce scale on ordinate by 600 units).

with the ratios H_2O_2/CrO_3 calculated therefrom. The value 2 thus obtained confirms the previous results of the extraction experiments.

The Rate of Formation and Composition of the Per-compound in Acetone–Water Mixtures.—When the solutions were mixed the optical density reached a maximum only after 5—10 min.;

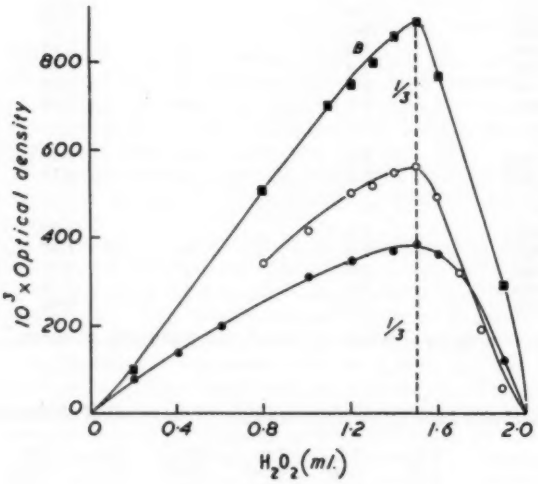


FIG. 2. *Job curves of 75% acetone–water mixtures.*

Variations with M/75 solns. of $K_2Cr_2O_7$ and H_2O_2: final acid concns.: ○, 0·01N-H_2SO_4 (Unicam); ●, 0·04M-HCl (Beckman DU); ■ (*B*), M/25-CrO_3 and M/50-H_2O_2, 0·025M-$HClO_4$.

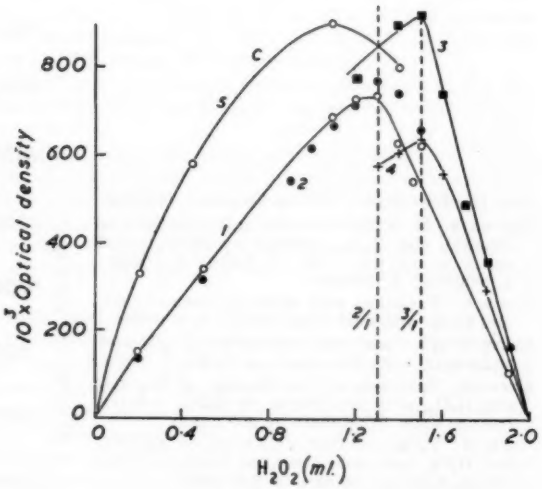
FIG. 3. *Job curves of 75% dioxan–water mixtures.*

Curves 1 and 2: Variations with M/50 solns. of Na_2CrO_4 and H_2O_2. Final acid concns.: 1, 0·05M-$HClO_4$; 2, 0·005M-$HClO_4$; 3 and 4, 0·01N-H_2SO_4.

Curve 3: Variations with M/50 solns. of $K_2Cr_2O_7$ and H_2O_2.

Curve 4: Variations with M/75 solns. of $K_2Cr_2O_7$ and H_2O_2.

Curve 5 (*c*): as curve 1 but with dioxan that contained peroxides.



the maximum remained constant for some time and then decreased according to an approximately first-order law.[10] For the experiments reported in the following section maximum values of the optical densities for each solution were recorded.

Composition of the Blue Per-compound in 75% Acetone–Water Solutions.—In Fig. 1 some curves obtained by Job's " continuous variations " method [1,7] are recorded. If sufficient acid (5×10^{-3}M-$HClO_4$, final concn.) is present, the maxima of the curves is at 65% H_2O_2, corresponding to a ratio $H_2O_2/CrO_3 = 2$. In solutions weaker in acid the maxima move towards

[10] Prakash and Rai, *Proc. Indian Acad. Sci.*, 1943, **18**, *A*, 1.

higher ratios, up to $H_2O_2/CrO_3 = 4$; also in the last solutions the colour develops rather slowly, impairing greatly the ease of measurements.

When the " variations " were made with equimolar solutions of hydrogen peroxide and potassium dichromate (Fig. 2), the maxima of the Job curves were at 75 mole-% H_2O_2, corresponding to the ratio $H_2O_2/K_2Cr_2O_7 = 3$, *i.e.*, $H_2O_2/CrO_3 = 1{\cdot}5$. Similar results were obtained with a chromium trioxide solution having twice the molar concentration of the hydrogen peroxide (curve *B*, Fig. 2). On the other hand, with a hydrogen peroxide solution of twice the molar concentration of the dichromate, the maximum of the curve occurred again at 65 mole-% H_2O_2 (curve *A*, Fig. 1).

Composition of the Blue Per-compound in 75% Dioxan–Water Solutions.—Job curves obtained in dioxan–water solutions are recorded in Fig. 3. The results were identical with those of the corresponding acetone solutions, with respect to variations with either chromate or dichromate solutions. Similar experiments [11] with dichromate in dioxan–water mixtures were made here previously by Avinur; his Job curves were identical with those now recorded.

Great care was taken to use peroxide-free dioxan; for example, in a mixture prepared from an old sample of dioxan, appreciable amounts of the perchromate were formed on acidifying the solution before any hydrogen peroxide had been added; with this sample the maximum on the Job curve shifted from 65 to 55 mole-% H_2O_2 (curve *C*, Fig. 3).

Discussion

The results with ethyl acetate extracts leave no doubt that the blue perchromic acid in this solvent is composed of two molecules of hydrogen peroxide to one molecule of chromiun trioxide. The analyses of the sexivalent chromium in the aqueous residues confirm this conclusion.

The blue per-compound formed in acidified acetone–water or dioxan–water mixtures shows identical absorption spectra with that of the ethyl acetate extract. Hence, one may assume that the per-compound in the mixed solvents is identical with that in the acetate extract. Yet the Job curves are apparently conflicting: the chromate–hydrogen peroxide " variations " indicate a ratio $H_2O_2/CrO_3 = 2$, and the dichromate–hydrogen peroxide " variations " a ratio of 1·5. Several possible causes for the discrepancy were tested and disproved: (*a*) The disturbing effect of peroxides in the organic solvents; (*b*) the acidity of the solutions (in less acid solutions the indicated ratio H_2O_2/CrO_3 rises, but does not fall below 2); (*c*) the original form of the stock solution of the chromium, whether monomeric (chromate) or dimeric (dichromate), does not affect the Job curves.

Recalling that the formation of the per-compound is a time-dependent reaction, we have no doubt that a considerable portion of the chromium present in the solution is not in the per-acid state at the moment of maximum optical density. This would cause the maximum of the Job curves to move towards a lower percentage of hydrogen peroxide, the shift being twice as large in the case of the dichromate variations. More precise measurements in greater volumes of solution support this view but do not prove it, owing to experimental difficulties. In fact, the exact maxima of the Job curves were blurred in these experiments.

Glasner's previous results in alcohol–water mixtures [3] seem to have suffered from a similar complication. It may therefore be concluded that the blue perchromic acid is composed of two molecules of hydrogen peroxide and one molecule of chromic acid, and that Schwarz and Giese's formulation [2] of the blue per-compound as CrO_5 (solvated) is correct.

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[11] Avinur, personal communication.

500. *Fluorinated Sulphonic Acids. Part I. Perfluoro-methane-, -octane-, and -decane-sulphonic Acids and their Simple Derivatives.*

By J. Burdon, I. Farazmand, M. Stacey, and J. C. Tatlow.

Perfluoro-methane-, -*n*-octane-, and -*n*-decane-sulphonyl fluoride were prepared from alkanesulphonyl chlorides by electrochemical fluorination.[1,2] Various derivatives of the fluorocarbonsulphonic acids were made. The long-chain acids were highly surface-active.

Recent patents assigned to the Minnesota Mining and Manufacturing Company [1] on the preparation of perfluoroalkanesulphonyl fluorides prompt us to publish some of our preliminary, very similar, results. The present paper describes the preparation, by the well-known electrochemical procedure of Simons,[2] of perfluoro-methane-, -*n*-octane-, and -*n*-decane-sulphonyl fluoride from the corresponding alkanesulphonyl chloride (which was made from the alkyl bromide *via* the sodium alkanesulphonate). The acid fluorides were then converted into simple derivatives of the fluorocarbonsulphonic acids.

Trifluoromethanesulphonyl fluoride was obtained in 50—60% yield (cf. Gramstad and Haszeldine [3]). Yields of perfluoro-*n*-octane- and -*n*-decane-sulphonyl fluoride were lower (12—15%) and large amounts of sulphur-free material, probably perfluoro-*n*-octane and perfluoro-*n*-decane, were obtained, together with smaller amounts of shorter-chain fluorocarbons and some polymeric residue. It appeared that the chlorine atoms of the sulphonyl chlorides were displaced electrolytically, since no apparent reaction took place with anhydrous hydrofluoric acid alone but a chlorine-containing gas was obtained during the fluorination of methanesulphonyl chloride. The yields of the fluorocarbonsulphonyl fluorides could probably be increased by more detailed individual studies.

Various salts were prepared from these acid fluorides by treatment with the appropriate aqueous metal hydroxide. The sodium and potassium salts of the C_8 and C_{10} acids were almost insoluble in water. However, though salts of strong acids, they were rather more soluble in ethanol than in the more highly ionising solvent, water. They differed from the corresponding perfluorocarboxylates in their much greater thermal stabilities. They melted below 330°, and were stable for long periods at 300° but decomposed in air at 350° (over a period of days) with the formation of sulphate ion: perfluorocarboxylic salts, on the other hand, decompose rapidly at about 250° to give olefins.[4]

The free C_1 acid [5,6] formed a hydrate sufficiently stable to be distilled from concentrated sulphuric acid. With phosphoric oxide the anhydrous acid gave the anhydride which decomposed partly after a few days, sulphur dioxide being evolved.

The C_8 and C_{10} acids were not isolated completely pure by distillation of mixtures of their salts with sulphuric acid because of their somewhat comparable volatilities. An aqueous solution of the C_{10} acid was prepared by treatment of a saturated solution of the sodium salt with an ion-exchange resin (Zeo-Karb 225). The free acid was converted, *in situ*, into its anilinium salt. An attempt to hydrolyse the C_8 sulphonyl fluoride with water at 160° for 60 hr. failed, no reaction taking place. Under milder conditions however, the C_1 fluoride was completely hydrolysed to the free acid. This difference in reactivity may have been due to the greater insolubility of the C_8 fluoride in water. These fluorosulphonic acids and their salts were very stable to acidic and to alkaline hydrolysis, and to strong oxidising agents. The perfluoro-*n*-octane- and -*n*-decane-sulphonic acids and

[1] Brice and Trott, U.S.P. 2,732,398; B.P. 758,467.
[2] Simons, "Fluorine Chemistry," Academic Press Inc., New York, 1950, Vol. I, p. 414; 1954, Vol. II, p. 340.
[3] Gramstad and Haszeldine, *J.*, 1956, 173.
[4] Hals, Reid, and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 4054.
[5] Haszeldine and Kidd, *J.*, 1954, 4228.
[6] *Idem*, *J.*, 1955, 2901.

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their salts are very good surface-active agents, and aqueous solutions containing only small amounts foam readily.

Trifluoromethanesulphonanilide was prepared by the action of aniline on the anhydride or the acid chloride. This anilide and the analogous amide had remarkable acidic properties; because of the powerful negative inductive effect of the trifluoromethanesulphonyl group, and possibly the negative hyperconjugative effect of the trifluoromethyl group, they were stronger acids than carbonic acid, and on titration with alkali gave end-points between pH 8·5 and 9·5 (in 0·006N-solution).

The anilides of the C_8 and the C_{10} acid were prepared from the acid fluorides and anilinomagnesium iodide in ether. Orthodox methods failed; for example, no reactions took place between aniline alone or aniline in pyridine and the acid fluorides, owing partly perhaps to the immiscibility of the reactants. The C_{10} anilide was not hydrolysed appreciably by boiling 5N-sodium hydroxide or by boiling 6N-hydrochloric acid. This stability reflects the behaviour of hydrocarbonsulphonanilides; fluorocarboncarboxyanilides are easily hydrolysed.

With sodium borohydride the C_8 and the C_{10} acid fluoride were reduced to the sulphinic acids, which were isolated as their *S*-benzylthiuronium salts. This appears to provide a new method of preparation of sulphinic acids.

Experimental

Apparatus.—The electrolytic cell was similar to that described by Simons.[2] The cell body was cylindrical and made of heavy gauge nickel (9 in. long × $3\frac{3}{8}$ in. diam. × $\frac{3}{16}$ in. thick) with a flange. The lid ($5\frac{3}{4}$ in. diam. × $\frac{1}{4}$ in. thick) was sealed with a Neoprene gasket and had two openings (one to introduce hydrofluoric acid and the starting material, and the other which led to the reflux condenser). It also carried the electrode assembly, which consisted of a vertical pack of alternate cathodes and slightly smaller anodes all made of nickel plate and mounted on two Polythene rods. The whole assembly was circular in cross-section with a total anode area of 350 sq. in. The cathode lead was connected directly to the lid, and hence the cell body, which was thus itself part of the cathode; the anode lead was insulated from the lid with a "Fluon" washer. The capacity of the cell with this electrode assembly in place was about 1 l. The cell itself was seated in a bath containing 30% ethylene glycol solution which was cooled by a standard refrigerator unit using "Freon 12" as the working liquid. The refrigerator coils first cooled the reflux condenser [a straight copper tube (2 ft. × $\frac{1}{2}$ in. int. diam.) in a vessel containing 30% glycol solution] and then the cell cooling-bath. The effluent gases passed up the condenser, and then into two traps kept at −78°. During a fluorination, the condenser was kept at about −12° and the cooling-bath at about −3°, but, even so, some hydrogen fluoride was invariably carried into the first receiver; this necessitated periodic additions of anhydrous hydrofluoric acid to the cell in order to keep up the liquid level (any large fall caused mild explosions).

Trifluoromethanesulphonyl fluoride was prepared essentially as described by others.[1,3] Methanesulphonyl chloride (100 g.) was electrolysed for 14 hr. at 18 amp. and 4·5 v. The reaction could be run continuously since the product distilled from the cell as it was formed.

Hydrolysis of Trifluoromethanesulphonyl Fluoride.—(*a*) The acid fluoride (58·5 g.), hydrated barium hydroxide (200 g.), and ice (100 g.), all cooled in liquid air, were introduced into a cooled (−78°) autoclave which was then sealed and heated at 90° for 12 hr. After acidification with sulphuric acid, neutralisation with barium carbonate, and filtration, the solution was evaporated *in vacuo* and the residue extracted with hot acetone. Evaporation of the filtered extracts left barium trifluoromethanesulphonate (78 g.) (Found: Ba, 31·1. Calc. for $C_2O_6S_2F_6Ba$: Ba, 31·5%).

When cold aqueous *S*-benzylthiuronium chloride was added to a solution of the barium salt, there was precipitated *S-benzylthiuronium trifluoromethanesulphonate*, m. p. 138—139° (from water) (Found: C, 34·4; H, 3·4. $C_9H_{11}O_3N_2S_3F_3$ requires C, 34·2; H, 3·5%).

(*b*) The acid fluoride (*ca.* 17 g.) was heated with water (60 ml.) in a sealed tube at 140° until two liquid layers were no longer present (40 hr.). Neutralisation with barium carbonate and treatment as in (*a*) gave barium trifluoromethanesulphonate (21·5 g.).

Trifluoromethanesulphonic Acid Derivatives.—(*a*) On being kept, the acid[5] formed, very

readily, a solid *monohydrate*, b. p. 120°/15 mm., m. p. *ca.* 45° (Found: equiv., 167. $CH_3O_4SF_3$ requires equiv., 168), which was white, crystalline, and very deliquescent, and could be distilled unchanged from concentrated sulphuric acid. It had infrared absorption peaks at 1037, 1180, and 1270 cm.$^{-1}$, in agreement with those found for the anhydrous acid.[5] The anhydrous and hydrated acids both gave, in the usual way (by precipitation from ethereal solutions), the same *anilinium salt*, m. p. 267—268° (from acetone–chloroform) (Found: C, 35·0; H, 3·2. $C_7H_8O_3NSF_3$ requires C, 34·6; H, 3·3%).

(*b*) The anhydrous acid (11·5 g.) and phosphoric oxide (11·5 g.) were mixed and kept at room temperature for 1 hr., and then the volatile products were distilled through a short Vigreux column to give trifluoromethanesulphonic anhydride (7·7 g.), b. p. 78—80° (Found: equiv., 286. Calc. for $C_2O_5S_2F_6$: equiv., 282). The compound was a mobile, hygroscopic liquid, readily hydrolysed by water, and had decomposed appreciably after being kept for a few days, with evolution of sulphur dioxide and formation of a brown, viscous, immiscible liquid. The anhydride was initially immiscible with aromatic hydrocarbons, ketones, and most carboxylic acids, but miscibility was gradually achieved in every case with the formation of dark-coloured tars.

(*c*) The anhydride (0·70 g.) was added to concentrated aqueous ammonia (30 ml.). After 12 hr. at 0° the solution was acidified and extracted with ether, and the extracts were dried ($MgSO_4$) and evaporated to leave a white residue which was sublimed at 100°/0·1 mm. to give trifluoromethanesulphonamide (0·25 g.), m. p. 117—118° (softens 112°) [cited value,[3] 119°] (Found: C, 8·0; H, 1·3%; equiv., 147. Calc. for $CH_2O_2NSF_3$: C, 8·05; H, 1·35%; equiv., 149). The equivalent weight was determined by electrometric titration of aqueous solutions (approx. 0·006N-amide against 0·05N-sodium hydroxide), the end-point lying between pH 8·5 and 9·5. An aqueous solution of the amide liberated carbon dioxide from saturated sodium hydrogen carbonate solution.

(*d*) A mixture of the acid chloride [5] (0·70 g.), aniline (1 ml.), pyridine (5 ml.), and dry ether (50 ml.) was kept at 13° for 20 hr. After being washed with dilute hydrochloric acid and water and dried ($MgSO_4$), this solution was evaporated to leave a residue which afforded trifluoromethanesulphonanilide (0·80 g.), m. p. 66—67° [from light petroleum (b. p. 40—60°)] (Found: C, 37·5; H, 2·7%; equiv., 225. Calc. for $C_7H_6O_2NSF_3$: C, 37·3; H, 2·7%; equiv., 225). The electrometric titration, done as before, showed an end-point between pH 8·5 and 9·5. The compound also liberated carbon dioxide from saturated sodium hydrogen carbonate solution.

(*e*) Treatment of the anhydride (1·0 g.) in ether with an excess of aniline gave an immediate precipitate of the anilinium salt which had m. p. 267—268°: the filtrate was treated as in (*d*) to give the anilide (0·52 g.), m. p. and mixed m. p. 66—67°.

Compounds mentioned previously [1] were the anhydride (b. p. 80·5°), the anilide (m. p. 65—66°), and the anilinium salt (m. p. 250—255°), no analyses being given.

n-*Octane- and* n-*Decane-sulphonyl Chloride*.—The parent alkyl bromide was treated [7] with concentrated aqueous sodium sulphite solution in an autoclave at 200°. The resulting sodium alkanesulphonate was filtered off, dried, and mixed at room temperature with an excess (2 mol.) of phosphorus pentachloride.[8] Heat was evolved, and after 2 hr. the liquid mixture was poured into ice-water, and the oil separated, washed, and dried. *n*-Octanesulphonyl chloride (yield 75—80%) had b. p. 90—91°/0·02 mm.; with concentrated aqueous ammonia it gave *n*-octanesulphonamide, m. p. 69—70° (from aqueous ethanol) (cited value,[9] 70—70·5°). n-*Decanesulphonyl chloride* (yield 75—80%) had m. p. 34° (from benzene) (Found: C, 49·7; H, 8·8. $C_{10}H_{21}O_2SCl$ requires C, 49·9; H, 8·8%). With aniline in pyridine it gave n-*decanesulphonanilide*, m. p. 51—52° (from aqueous ethanol) (Found: C, 64·4; H, 9·1. $C_{16}H_{27}O_2NS$ requires C, 64·6; H, 9·15%).

Preparation of Perfluoro-n-*octanesulphonyl Fluoride*.—In a typical experiment, *n*-octanesulphonyl chloride (205 g.) was fluorinated for 190 hr. at 14 amp. and 5·0 v. The cell was drained and the heavier layer was separated from the hydrofluoric acid, washed with water, and dried ($MgSO_4$). The product (223 g.) was fractionally distilled through a 1 ft. column packed with Dixon gauze spirals. Boiling commenced at 29° and small fractions were obtained at 57° and 82°; these sulphur-free fractions were probably perfluoro-*n*-hexane and perfluoro-*n*-heptane, respectively. A large fraction (41 g.), b. p. 103°, was probably perfluoro-*n*-octane.

[7] Reed and Tartar, *J. Amer. Chem. Soc.*, 1935, **57**, 570.
[8] Carius, *Annalen*, 1860, **114**, 140.
[9] Kharasch and Mosher, *J. Org. Chem.*, 1952, **17**, 453.

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Analytical gas chromatography on dinonyl phthalate–kieselguhr (1 : 2) at 80° with a rate of flow of nitrogen of 0·8 l./hr. showed that the combined sulphur-free distillates (64 g.) contained at least four compounds, probably the normal C_5, C_6, C_7, and C_8 fluorocarbons, the last being present in largest amount.

Continued fractionation gave perfluoro-*n*-octanesulphonyl fluoride (72 g.), b. p. 154°, n_D^{14} 1·3037 (Found : C, 19·2; F, 67·7. Calc. for $C_8O_2SF_{18}$: C, 19·1; F, 68·1%) (cited values [1] were b. p. 154·5° and n_D^{25} 1·2993 for this compound). The fractionation residue (33 g.) was a viscous, dark, fuming liquid, which was probably polymeric.

Salts of Perfluoro-n-*octanesulphonic Acid.*—The acid fluoride (5·0 g.) was treated with 10N-sodium hydroxide for 17 hr. at 15°, with occasional stirring. The precipitate was filtered off and recrystallised from ethanol to give *sodium perfluoro*-n-*octanesulphonate* (4·3 g.), m. p. 327—330° (Found : C, 18·1; F, 61·5. $C_8O_3SF_{17}Na$ requires C, 18·4; F, 61·9%). The potassium salt, prepared in the same way, had m. p. 277—280° (Found : C, 17·9; F, 60·1. Calc. for $C_8O_3SF_{17}K$: C, 17·85; F, 60·0%). Both these salts decomposed at 350° over a period of several days with the formation of sulphate ion. Saturated aqueous solutions formed very stable foams which could not be dispersed with either octyl alcohol or a Silicone anti-foaming preparation.

The S-*benzylthiuronium salt* was prepared from a hot aqueous solution of the sodium salt. Recrystallised from aqueous ethanol, it had m. p. 111—112° (Found : C, 28·7; H, 1·8; F, 48·0. $C_{16}H_{11}O_3N_2S_2F_{17}$ requires C, 28·8; H, 1·7; F, 48·5%).

Preparation of Perfluoro-n-*decanesulphonyl Fluoride.*—*n*-Decanesulphonyl chloride (160 g.) was electrolysed, as before, at 15 amp. and 5·2 v for 129 hr. Fractionation of the product (263 g.), initially at atmospheric pressure (for b. p.s < 135°) and finally at 27 mm., gave sulphur-free material (106 g.) which appeared to contain at least five components, probably the normal C_6, C_7, C_8, C_9, and C_{10} fluorocarbons, and then perfluoro-*n*-decanesulphonyl fluoride (48 g.), b. p. 90—91°/27 mm., which crystallised. After recrystallisation from ether–ethanol the pure *fluoride* had m. p. 57—59° (Found : C, 19·8; F, 69·2. $C_{10}O_2SF_{22}$ requires C, 19·9; F, 69·4%). The fractionation residue (47 g.) was a dark viscous tar.

Salts of Perfluoro-n-*decanesulphonic Acid.*—The *sodium salt*, m. p. 322—325° (Found : C, 19·0; F, 63·7. $C_{10}O_3SF_{21}Na$ requires C, 19·3; F, 64·1%), the *potassium salt*, m. p. 280—287° (Found : C, 18·8; F, 62·0. $C_{10}O_3SF_{21}K$ requires C, 18·8; F, 62·5%), and the S-*benzylthiuronium salt*, m. p. 134—135° (Found : C, 28·2; H, 1·4. $C_{18}H_{11}O_3N_2S_2F_{21}$ requires C, 28·2; H, 1·4%), were prepared as described above. The sodium and potassium salts were almost insoluble in cold ethanol (*ca.* 0·6%), and even less soluble in cold water (*ca.* 0·2%), as were the C_8 salts. They were also excellent foaming agents, and had thermal stabilities similar to those of the C_8 salts.

A solution of the sodium salt (2·0 g.) in water (4 l.) was passed down a column of ion-exchange resin (Zeo-Karb 225). The aqueous effluent was concentrated to 50 ml., aniline (5 ml.) was added, and the precipitate was filtered off and recrystallised from aqueous ethanol to give *anilinium perfluoro*-n-*decanesulphonate* (1·6 g.), m. p. 213—216° (decomp.) (Found : C, 28·1; H, 1·0; F, 57·3. $C_{16}H_8O_3NSF_{21}$ requires C, 27·7; H, 1·2; F, 57·55%).

Preparation of C_8 *and* C_{10} *Anilides.*—The C_8 acid fluoride (5·0 g.) was added to a solution of anilinomagnesium iodide [made from ethyl iodide (3·5 ml.), magnesium (1·0 g.), and aniline (4 ml.) in ether (100 ml.)] and the mixture was refluxed for 1 hr. Dilute sulphuric acid was added and the ether layer was separated, dried ($MgSO_4$), and evaporated. Recrystallisation of the residue from benzene afforded *perfluoro*-n-*octanesulphonanilide* (2·9 g.), m. p. 101—102° (Found : C, 29·5; H, 1·3; F, 56·2. $C_{14}H_6O_3NSF_{17}$ requires C, 29·2; H, 1·05; F, 56·15%).

In the same way the C_{10} acid fluoride (2·0 g.) afforded the corresponding *anilide* (1·3 g.), m. p. 117—118° [from light petroleum (b. p. 60—80°)] (Found : C, 28·3; H, 1·0; F, 59·6. $C_{16}H_6O_3NSF_{21}$ requires C, 28·5; H, 0·9; F, 59·1%). After being refluxed for 6 hr. with 5N-sodium hydroxide (100 ml.) this compound (0·20 g.) was recovered, by acidification of the solution and extraction with ether, in almost quantitative yield (0·19 g.). With boiling 6N-hydrochloric acid the compound slowly distilled from the solution in the steam and was deposited unchanged in the condenser.

Preparation of Sulphinic Acids.—To a stirred solution of the C_8 acid fluoride (1·0 g.) in ether (75 ml.), a solution of sodium borohydride (0·50 g.) in ethanol (75 ml.) was added dropwise. A vigorous reaction took place with the evolution of gaseous products. After 15 hr. at 16°, acetone (5 ml.) was added to destroy the excess of sodium borohydride. After a further 2 hr.

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at room temperature, the solution was concentrated *in vacuo* at 15° to 25 ml. Water (25 ml.) was added, followed by sufficient 2N-hydrochloric acid to bring the pH to 7. A saturated aqueous solution of *S*-benzylthiuronium chloride was added and the resulting precipitate was filtered off and recrystallised twice from aqueous ethanol to give S-*benzylthiuronium perfluoro*-n-*octanesulphinate* (0·9 g.), m. p. 129—130° (Found: C, 29·9; H, 1·4; F, 50·2. $C_{16}H_{11}O_2N_2S_2F_{17}$ requires C, 29·55; H, 1·7; F, 49·7%).

In the same way the C_{10} acid fluoride (1·0 g.) gave S-*benzylthiuronium perfluoro*-n-*decanesulphinate* (1·1 g.), m. p. 140—141°, depressed to 119—123° on admixture with the corresponding sulphonic acid derivative (Found: C, 28·9; H, 1·6; F, 54·0. $C_{18}H_{11}O_2N_2S_2F_{21}$ requires C, 28·8; H, 1·5; F, 53·2%).

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501. *Some Factors which might affect the Accuracy of the Iodometric Estimation of Penicillin.*

By J. E. BANFIELD.

Iodide concentration, and other factors, are shown to affect the results of iodometric estimation of penicillin.

THE iodometric estimation of penicillin [1,2] is not stoicheiometric; the uptake of iodine after hydrolysis has been reported [1] to be 8·97 equivs. per mole (in 15 min. at room temperature). During another investigation it was noted that variation from the standard method of estimation [2] sometimes led to considerable inaccuracy.

Rates of uptake of iodine at various iodide-ion concentrations and pH values have been determined at 0°. Graphs of the results (see Figure) show breaks which indicate that a number of consecutive reactions are involved, and that variation of the conditions, particularly of the iodide concentration, may affect different stages of the reaction in different ways.

At a low iodide concentration of 0·075M the uptake of iodine per mole of penicillin is not affected appreciably by a two-fold dilution of the reaction mixture. In solutions of much higher iodide concentration (1·5M), however, the effect of a two-fold dilution is to increase the rate of uptake at intermediate times. An increased rate of reaction on dilution of the mixture is also observed (at pH 5·33) when potassium chloride (final concentration 1·5M) is added to the diluted mixture, in which case the ionic strength of the solution is somewhat higher than in the undiluted mixture.

Katzin and Gebert [3] have investigated the iodine–iodide–tri-iodide equilibrium in the range of iodide concentrations 0·02—0·08M and at various ionic strengths. They find that changing the ionic strength in the range 0·1—1 has little effect on the equilibrium constants K_c at 20° and 25°, although the activity coefficients vary somewhat.

$$[I_3^-]K_c = [I_2][I^-] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (i)$$

Results of the present investigation are explicable if each intermediate product P_n is oxidised at such a rate that

$$-\partial[P_n]/\partial t = [P_n] \cdot \Phi_n([I_2], -) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (ii)$$

where Φ_n is a function which may depend on pH, etc. Provided that conditions (i) and (ii) are fulfilled simultaneously for all steps in the reaction sequence, the uptake of iodine per mole of penicillin will be independent of dilution, for all values of t.

[1] Alinico, *Ind. Eng. Chem. Anal.*, 1946, **18**, 619.
[2] Ministry of Health Conference, *Analyst*, 1949, **74**, 550.
[3] Katzin and Gebert, *J. Amer. Chem. Soc.*, 1955, **77**, 5814.

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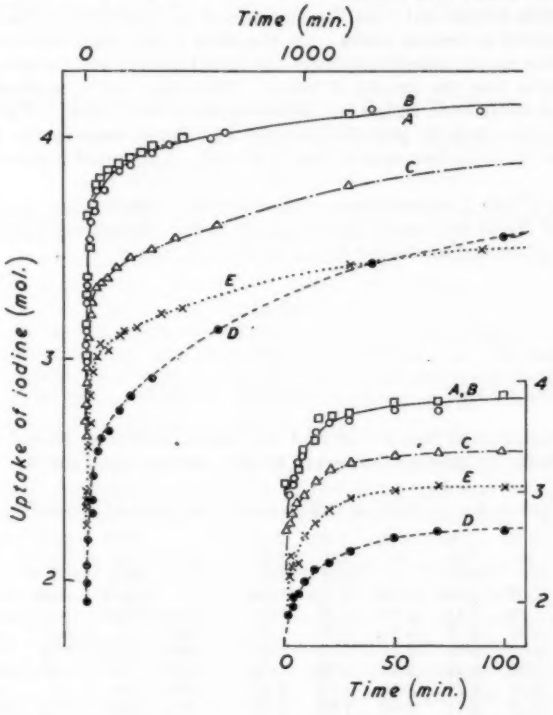
In solutions of higher iodide concentration, however, the effects of both the formation of higher polyiodide ions and of larger changes in the activity coefficients must become more important. Although conclusions concerning a mechanism derived from rates measured in such concentrated solutions are not necessarily valid, the faster reaction in the dilute solution might indicate a reversible reaction involving iodide ions.

Rate of uptake of iodine in runs B—E *of Table* 1, *and* (A) *under conditions of section* (i).



Estimation of penicilloic acid during the hydrolysis of penicillin by enzymes requires that either the enzyme be inactivated or that the time of contact with iodine be reduced to a minimum. When the standard method of estimation is varied, it seems important to determine both the amount and the rate of uptake of iodine at a number of penicilloic acid concentrations, for the final iodine–iodide ratio will differ from case to case.

Experimental

Materials.—Penicillin G sodium salt (crystalline; Commonwealth Serum Laboratories, Melbourne, Australia) (6·066 g.) was treated in water with M-sodium hydroxide (50 ml.) at 50° for 30 min.; the mixture was cooled, adjusted to pH 7·0 with 1·1M-hydrochloric acid and made up to 250 ml. with water. One drop of chloroform was added, and the mixture was kept at 4°. The supernatant liquid remained clear for several months. 0·5M-Phosphate buffer solutions were prepared from phosphoric acid, potassium dihydrogen phosphate, and disodium hydrogen phosphate, and the pH values were determined with both glass and quinhydrone electrodes. 0·05M-Iodine containing potassium iodide (50·0 g./l.) was used. Solutions containing appreciably less iodide deposited iodine on long storage at 0°.

Kinetic Measurements.—Runs were carried out in volumetric flasks which were cooled by immersion in ice–water contained in a heavily lagged bath. The temperature of the mixtures

varied between 0° and 1° during the reaction, but essentially no better temperature control was obtained when the ice-water was stirred. Runs, but not all readings, were duplicated.

(i) 0·5M-Phosphate buffer solution (pH 6·92; 120·0 ml.), water (20·0 ml.), and the penicillin hydrolysis mixture (10·00 ml.) were mixed and kept overnight in the ice-water bath. 0·05M-Iodine (50·0 ml.), cooled similarly, was added, and the whole mixed rapidly. Aliquot parts (10·00 ml.) were removed at intervals and added immediately to known amounts of sodium thiosulphate solution. The mixture was cooled by the addition of crushed ice, and the excess of thiosulphate was titrated with iodine.

Parallel runs were carried out with the omission of the penicillin. The loss of iodine was negligible over a period of several weeks. On the other hand, oxidation of iodide in the more acidic conditions was rapid immediately after the initial mixing and in some cases this oxidation was more rapid than the uptake of iodine. This effect could be eliminated by flushing the flasks with carbon dioxide before the iodine solution was added. The uptake of iodine (as moles of iodine per mole of penicillin) is plotted against time in the Figure (curve A). Uptake after 16 hr. at room temperature was 4·42 mol. The initial iodine concentration was 0·01354M-I_2.

(ii) Runs *B*—*E* (Table 1) were carried out as described in section (i). In each case penicillin hydrolysis mixture (10·00 ml.) and 0·5M-phosphate buffer solution were present. The uptake of iodine per mole of penicillin is shown in curves *B*, *C*, *D*, and *E*.

TABLE 1.

Run	*B*	*C*	*D*	*E*
Water added (ml.)	220	20	20	220
KI added (g.)	—	10·0	50·0	50·0
Initial [I] (M)	0·00684	$0·0135_1$	$0·0127_1$	0·00660

(iii) Results of additional runs at different pH values, with 0·5M-phosphate buffer solution (120 ml.) and penicillin hydrolysis mixture (10·00 ml.), are given in Table 2.

TABLE 2. *Uptake of iodine (moles per mole of penicillin).*

pH of buffer	5·33	5·33	3·42	3·42	3·42		5·33	5·33	3·42	3·42	3·42
H_2O added (ml.)	20	220	20	20	220		20	220	20	20	220
KI added (g.)	50·0	50·0 *	—	50·0	50·0		50·0	50·0 *	—	50·0	50·0
[I] (10^3M)	12·76	6·36	12·25	11·49	5·96		12·76	6·36	12·25	11·49	5·96
Time (min.): 2	1·93	2·11	3·18	1·25	1·14	250	3·19	—	3·90	—	2·56
3	2·02	2·19	3·28	1·26	1·41	360	—	—	—	2·64	—
4	2·08	2·28	3·35	1·46	1·57	400	3·29	3·79	—	—	2·79
6	2·20	2·42	3·43	1·66	1·73	450	—	—	3·96	—	2·77
9	2·31	2·56	3·49	1·77	1·87	600	—	—	—	2·78	2·93
14	2·44	2·71	3·60	1·92	1·98	700	3·45	3·94	3·98	—	—
20	2·60	2·86	3·64	1·99	2·00	1300	—	4·06	4·00	3·11	3·36
30	2·71	3·02	3·72	2·06	2·12	1800	—	—	4·01	—	3·58
50	2·85	3·20	3·75	2·13	2·21	3000	3·86	4·17			
70	—	3·29	3·78	2·20	2·32	7600	—	4·34			
100	2·99	3·37	3·81	2·28	2·54	14,600	4·38	—			
150	3·07	3·50	—	—	2·41	17,300	—	4·57			
160	—	—	3·86	—	—	23,000	4·48	—			
200	—	3·62	—	2·44	2·56						

* KCl (47·5 g.) was also added.

(iv) 0·5M-Phosphate buffer solution (pH 3·42; 120·0 ml.), water (220 ml.), and penicillin hydrolysis mixture (10·00 ml.) were treated as described in (i). After each titration the pH of the aliquot portion was determined with a glass electrode system. The uptake of iodine is given in Table 3.

TABLE 3.

Time (min.)	2	3	4	6	9	14	21	30	50
I uptake (mol.)	2·97	3·12	3·25	3·37	3·49	3·61	3·68	3·73	3·80
pH	3·45	3·48	3·45	3·49	3·44	3·38	3·42	3·46	3·45
Time (min.)	70	100	150	200	375	580	1300	1800	
I uptake (mol.)	3·83	3·86	3·89	3·90	3·94	3·97	4·01	4·01	
pH	3·46	—	3·40	3·40	3·43				

Initial iodine concentration 0·00609M-I_2.

(v) To a mixture of 0·1M-phosphate buffer solution (20 ml.) and crushed ice was added 0·00856M-penicillin hydrolysis mixture (10·00 ml.), and the mixture was titrated with 0·005M-iodine. The uptake of iodine (mol.) at various pH values was: pH 7·0, 1·26; pH 6·0, 1·06; pH 5·0, 1·01; pH 4·0, 1·15.

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502. *Standard Potentials in Aqueous Organic Media: a General Discussion of the Cell* H_2(Pt)|HCl|AgCl–Ag.

By D. FEAKINS and C. M. FRENCH.

Relations for the standard potential of the cell H_2(Pt)|HCl|AgCl–Ag in various aqueous organic media, based on the Born equation, are briefly reviewed, and the limitations of this method noted. A new stoicheiometric relationship is developed, based on a simple treatment of ion solvation in liquid mixtures. The resulting equation shows that a plot of the standard potential $E_0°$ on the molar scale should be linearly related to the logarithm of the volume fraction ϕ_w of water in the solvent medium. The correlation achieved experimentally is considerably better than anything obtained with plots based on the Born equation, and is free from marked solvent effects. Certain observed deviations are discussed.

FOLLOWING work on aqueous ketone and glycol solutions (cf. *J.*, 1957, 2284), we can discuss the standard potentials of the cell H_2(Pt)|HCl|AgCl–Ag in a large number of aqueous solutions of the commoner water-soluble organic substances, particularly where the water content is high.

In Table 1 are given all the available standard potentials of the cell for such systems on the molal ($E_m°$), molar ($E_c° = E_m° + 2k \log d_0$), and mole fractional [$E_N° = E_m° - 2k \log (1000/M_{xy})$] scales ($k = 2·3026\ RT/F$, d_0 = density of pure solvent mixture $M_{xy} = 100/[X/M_x + (100 - X)/M_y]$ = mean molecular weight of solvent (X = weight % of organic substance of molecular weight M_x, and M_y = molecular weight of water). Values of the dielectric constant ε, and of the density d_0 of each mixture are recorded. Where not given by the original author, the values of ε are taken from Åkerlöf's data,[1] and the d_0 values from International Critical Tables or from Griffiths's data.[2,3] The mole fraction of water, N_w, has been calculated for each mixture.

The difference between the standard potentials, ${}^wE°$ in water and ${}^sE°$ in another solvent, is related to a free-energy difference ΔG by the equations

$$-\Delta G = F({}^wE° - {}^sE°) = -2RT \ln a_1/a_2 = -2RT \ln f_1c_1/f_2c_2$$

ΔG is the difference in solvation energies of hydrogen chloride in the two solvents, referred to standard conditions in the gas phase and the standard state in the given solvent, $_1$ and f_2 are mean ion-activity coefficients referred to a standard state of unity at infinite dilution in pure water, *i.e.*, $f_1 = 1$. By the definition of standard potential, interionic attractions are eliminated, and we are concerned solely with ion–solvent interactions.

It would be convenient to choose the standard state such that the work done in transferring the ions, considered uncharged, is zero; in other words, that terms of the type $2RT \ln c_1/c_2$ vanish. Classically this is assumed to be the case if the mole fraction of

[1] Åkerlöf, *J. Amer. Chem. Soc.*, 1937, **59**, 2098.
[2] Griffiths, *J.*, 1952, 1326.
[3] *Idem, ibid.*, 1954, 860.

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TABLE 1. *Standard potentials of binary aqueous systems at 25°.*

Organic component	X	N_w	d_0	ε	$E_m°$	$E_N°$	$E_c°$ (See p. 2583)	Ref.
Acetone	5	0·9839	0·9904	75·9	0·2190	$0·0144_5$	0·2185	*a*
	10	0·9667	0·9838	73·0	0·2156	0·0129	0·2148	*a*
	20	0·9280	0·9697	67·0	$0·2079_5$	$0·0091_5$	$0·2063_5$	*a*
	40	0·8286	0·9367	54·6	$0·1859_5$	$-0·0038_5$	0·1824	*a*
	50	0·7632	0·9173	48·2	0·158	−0·027	0·154	*b*
	90	0·2637	0·8160	24·0	−0·034	−0·190	−0·044	*b*
	100	0	0·7850	19·1	−0·53	−0·78	−0·542	*c*
MeEtCO	10	0·9729	0·9845	71·8	$0·2153_5$	$0·0129_5$	0·2144	*d*
	20	0·9412	0·9703	64·9	0·2078	0·0098	$0·2064_5$	*d*
Methanol	10	0·9412	0·9799	74·0	$0·2154_5$	0·0112	0·2144	*e*
	20	0·8767	0·9644	69·2	0·2088	0·0071	$0·2069_5$	*e*
	43·3	0·6996	0·9248	58·0	0·1941	−0·0022	0·1901	*f*
	64	0·5001	0·8814	48·0	0·1764	−0·0130	0·1699	*f*
	84·2	0·2502	0·8333	38·2	0·1319	−0·0508	0·1255	*f*
	94·2	0·0987	0·8042	33·9	0·0840	−0·0950	0·0728	*f*
	100	0	0·7865	31·5	−0·0101	−0·1869	−0·0224	*f*
	10	0·9412	0·9799	74·18	0·2155	0·0114	0·2145	*g*
	20	0·8768	0·9645	69·99	0·2094	0·0077	0·2076	*g*
	40	0·7275	0·9319	60·94	0·1968	0·0003	0·1932	*g*
	60	0·5426	0·8914	51·67	0·1818	−0·0089	0·1759	*g*
	80	0·3059	0·8425	42·60	0·1492	−0·0350	0·1404	*g*
	90	0·1650	0·8156	37·91	0·1135	−0·0672	0·1030	*g*
	94·2	0·0987	—	35·76	0·0841	−0·0950	—	*g*
	100	0	0·7864	32·66	−0·0099	−0·1867	−0·0223	*g*
Ethanol	10	0·9583	0·9804	72·8	0·2144	0·0112	$0·2136_5$	*h*
	20	0·9109	0·9664	67·0	$0·2073_5$	0·0076	0·2056	*h*
	30	0·8566	0·9507	61·1	$0·2003_5$	0·0043	0·1981	*i*
	40	0·7932	0·9315	55·0	$0·1945_5$	0·0025	0·1909	*i*
	50	0·7189	0·9098	49·0	0·1859	$-0·0018_5$	0·1810	*i*
	71·9	0·5000	0·8588	37·0	0·1554	−0·0214	0·1476	*j*
	88·5	0·2500	0·8176	27·4	0·1053	−0·0358	0·0950	*j*
	98	0·0500	0·7912	25·1	0·0215	−0·1382	0·0095	*j*
	100	0	0·7851	24·3	−0·0760	−0·2341	−0·0884	*j*
Propan-1-ol	10	0·9668	0·9811	71·8	0·2141	0·0115	0·2132	*k*
	20	0·9296	0·9670	64·9	$0·2066_5$	0·0080	0·2049	*k*
Propan-2-ol	5	0·9832	0·9891	74·9	$0·2180_5$	0·0135	$0·2174_5$	*l*
	10	0·9668	0·9812	71·4	$0·2138_5$	0·0112	0·2127	*l*
	20	0·9296	0·9669	64·1	$0·2063_5$	$0·077_5$	0·2046	*l*
Ethylene glycol	5	0·9848	1·005	76·9	$0·2190_5$	$0·0145_5$	$0·2192_5$	*m*
	10	0·9689	1·010	75·6	0·2161	0·0136	0·2166	*n*
	15	0·9514	1·016	74·2	0·2133	$0·0127_5$	0·2141	*m*
	20	0·9322	1·023	72·8	0·2101	0·0117	$0·2112_5$	*n*
	30	0·8890	1·035	69·8	0·2036	$0·0095_5$	0·2053	*m*
	40	0·8377	1·049	66·6	0·1972	0·0080	$0·1996_5$	*o*
	60	0·7009	1·075	59·4	0·1807	0·0028	0·1884	*o*
Propylene glycol	10	0·9745	1·0046	74·2	$0·2150_5$	0·0128	0·2153	*m*
	20	0·9440	1·0128	70·7	$0·2077_5$	$0·0099_5$	0·2084	*m*
2 : 3-Butylene glycol	10	0·9785	1·0024	73·2	0·2144	$0·0123_5$	0·2145	*m*
	20	0·9524	1·0089	69·0	0·2067	$0·0088_5$	0·2067	*m*
Glycerol	4·9	0·9900	1·009	77·1	0·2196	0·0153	$0·2200_5$	*p*
	10	0·9789	1·021	75·5	0·2165	0·0145	$0·2175_5$	*q*
	21·2	0·9500	1·048	72·5	0·2084	0·0117	0·2108	*p*
	30	0·9226	1·070	70·1	0·2022	0·0100	0·2057	*q*
	50	0·8364	1·120	64·0	0·1840	0·0040	0·1896	*r*
D-Glucose	5	0·9943	1·003	77·3	$0·2186_5$	0·0146	$0·2187_5$	*s*
	10	0·9894	1·007	76·1	0·2142	0·0127	$0·2144_5$	*s*
	20	0·9754	1·016	73·4	0·2045	0·0083	0·2053	*s*
	30	0·9587	1·025	70·5	$0·1935_5$	0·0033	$0·1947_5$	*s*
D-Fructose	5	0·9943	1·003	77·3	0·2190	0·0150	$0·2191_5$	*t*
	10	0·9894	1·007	76·1	$0·2150_5$	$0·0135_5$	0·2154	*t*
1 : 4-Dioxan	20	0·9513	1·014	60·8	$0·2030_5$	$0·0055_5$	$0·2037_5$	*u*
	45	0·8567	1·032	38·5	0·1635	−0·0201	0·1652	*u*
	70	0·6770	1·038	17·7	$0·0639_5$	−0·1006	0·0657	*u*
	82	0·5177	1·034	9·5	−0·0413	−0·1934	−0·0396	*u*

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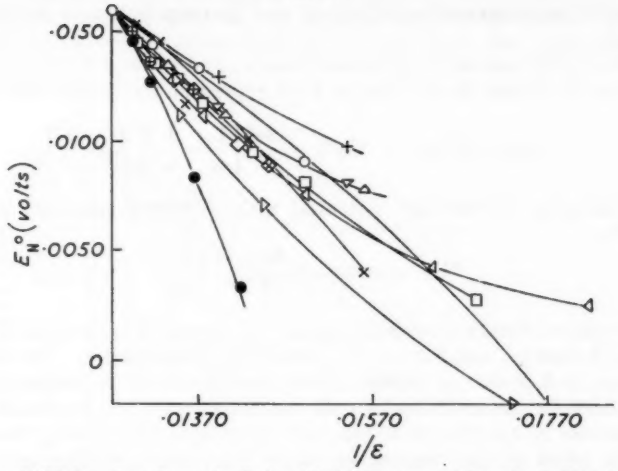
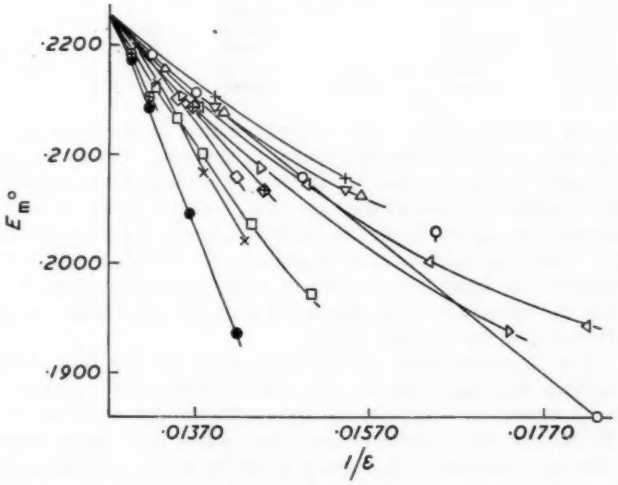
FIG. 1.



For all Figures.—◎ Water, ○ acetone, + ethyl methyl ketone, ▷ methanol, ◁ ethanol, ▽ propan-1-ol, △ propan-2-ol, □ ethylene glycol, ◊ propylene glycol, ⧫ 2 : 3-butylene glycol, × glycerol, ♀ dioxan, ● glucose, ⁞ glucose (dihydrate), ⊕ fructose.

FIG. 2.



(*a*) Feakins and French, *J.*, 1956, 3168; (*b*) Izmailov and Zabara, *Zhur. fiz. Khim.*, 1946, **20**, 165 (from measurements with a quinhydrone electrode); (*c*) Everett and Rasmussen, *J.*, 1954, 2812; (*d*) Feakins and French, preceding paper; (*e*) Harned and Thomas, *J. Amer. Chem. Soc.*, 1935, **57**, 1666; 1936, **58**, 761; (*f*) Austin, Hunt, Johnson, and Parton, unpublished, see Robinson and Stokes, "Electrolyte Solutions," Butterworths Scientific Publications, London, 1955, p. 457; (*g*) Oiwa, *J. Phys. Chem.*, 1956, **60**, 754; (*h*) Harned and Calmon, *J. Amer. Chem. Soc.*, 1939, **61**, 1491; (*i*) Harned and Allen, *J. Phys. Chem.*, 1954, **58**, 191; (*j*) Butler and Robertson, *Proc. Roy. Soc.*, 1929, **125**, *A*, 694; (*k*) Claussen and French, *Trans. Faraday Soc.*, 1955, **51**, 708; (*l*) Moore and Felsing, *J. Amer. Chem. Soc.*, 1947, **69**, 1076; (*m*) Crockford, Knight, and Staton, *ibid.*, 1950, **72**, 2164; (*n*) Claussen and French, *Trans. Faraday Soc.*, 1955, **51**, 1124; (*o*) Knight, Masi, and Roesel, *J. Amer. Chem. Soc.*, 1946, **48**, 661; (*p*) Lucasse, *Z. phys. Chem.*, 1926, **121**, 254; (*q*) Knight, Crockford, and James, *J. Phys. Chem.*, 1953, **57**, 463; (*r*) Harned and Nestler, *J. Amer. Chem. Soc.*, 1946, **68**, 665; (*s*) Williams, Knight, and Crockford, *ibid.*, 1950, **72**, 1277; (*t*) Crockford and Sahnovsky, *ibid.*, 1951, **73**, 4177; (*u*) Harned *et al.*, *ibid.*, 1936, **58**, 1908; 1938, **60**, 334, 336, 339, 2128, 2130, 2133; 1939, **61**, 44, 48, 49.

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the acid is the same in both solvents. This assumption will not always be justified, since most of the liquid mixtures are far from ideal, and the contribution to ΔG from this source might be large.

By considering the ions to be spheres of radii r_+ and r_- respectively, in a uniform dielectric medium, we obtain the well-known Born expression for the free energy of transfer:

$$-\Delta G = F[{}^{w}E_N^\circ - {}^{s}E_N^\circ] = \frac{Ne^2}{2}\left[\frac{1}{\varepsilon_s} - \frac{1}{\varepsilon_w}\right]\left[\frac{1}{r_+} + \frac{1}{r_-}\right]$$

For the variation of standard potential with dielectric constant, ε, we find on rearranging that

$${}^{s}E_N^\circ = \text{const.} - \frac{Ne^2}{2F}\sum\frac{1}{r}\left(\frac{1}{\varepsilon_s}\right) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Hence the plot of standard potential against $1/\varepsilon$ should be a straight line.

Figs. 1 and 2 show plots of E_N° and E_m° respectively against $1/\varepsilon$. The salient features of such plots are as follows. (*a*) Distinct plots, usually smooth curves and rarely straight lines, are obtained for the solutions for each organic solvent. (*b*) In general the decrease in E° with increase in $1/\varepsilon$, though of the right order, is much less than predicted by the Born equation when we use reasonable values [*e.g.*, the crystallographic radii, when $\Sigma 1/r = 1{\cdot}2$ Å^{-1}, or the experimental mean distance of closest approach (4·3 Å) when

TABLE 2. *Activity of water in glucose solutions and solvation numbers.*

N_w	p (mm. Hg)	$a_w = p/p^\circ$	y	N_w	p (mm. Hg)	$a_w = p/p^\circ$	y
1	23·756 = p°	1	—	0·9050	21·117	0·8888	1·53
0·9882	23·476	0·9882	—	0·8909	20·668	0·8700	1·47
0·9492	22·563	0·9498	—	0·8696	19·943	0·8384	1·48
0·9239	21·727	0·9146	(1·4)	0·8402	19·002	0·7995	1·27
0·9066	21·151	0·8903	1·59	0·8060	17·751	0·7477	1·19

$\Sigma 1/r = 0{\cdot}9$ Å^{-1}] for the ionic radii. The only values that fit the Born plot at all well are those of glucose solutions which are exceptional in this respect. (*c*) The curves fall into fairly distinct families, a feature that is particularly evident on examination of the E_m° against $1/\varepsilon$ curves, where the rate of decrease of E_m° with increase in $1/\varepsilon$ depends on the number of functional groups in the organic molecule, being larger the greater the number of such groups. Here the monofunctional ketones show a fairly close relation to the monohydric alcohols, at least in solutions of high dielectric constant. This relation disappears on the E_N° versus $1/\varepsilon$ curves where, for example, there is an unexpected relation between the glycerol and the acetone curves.

Scatchard [4] first suggested that the Born equation for the free energy of transfer required modification if it were assumed that the hydrogen ion is present as the species H_3O^+. It can be shown, for example by arguments similar to those developed below (see also ref. 5), that in the transfer of ions from water to a water–organic compound mixture there will be an increase of free energy given by $\Delta G = -RT \ln a_w$, where a_w is the activity of water in the solvent mixture. If the remaining free energy is determined by the Born expression, then

$$F[{}^{w}E_N^\circ - {}^{s}E_N^\circ] = \frac{Ne^2}{2}\left[\frac{1}{\varepsilon_s} - \frac{1}{\varepsilon_w}\right]\sum\frac{1}{r} - RT \ln a_w$$

This can be rearranged in the form

$${}^{s}E_N^\circ - (RT/F) \ln a_w = \text{const.} - \frac{Ne^2}{2F}\sum\frac{1}{r}\left(\frac{1}{\varepsilon}\right) \quad . \quad . \quad . \quad . \quad . \quad (2)$$

[4] Scatchard, *J. Amer. Chem. Soc.*, 1925, **47**, 2098.
[5] Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publishing Corporation, New York, 1956, 2nd edn., p. 337.

For most of the solutions considered, the partial-pressure data available indicate that, provided the concentration of water in the aqueous organic medium is high, the mole fraction of water N_w can be substituted for a_w. Equation (2) then suggests the plot of

FIG. 3.

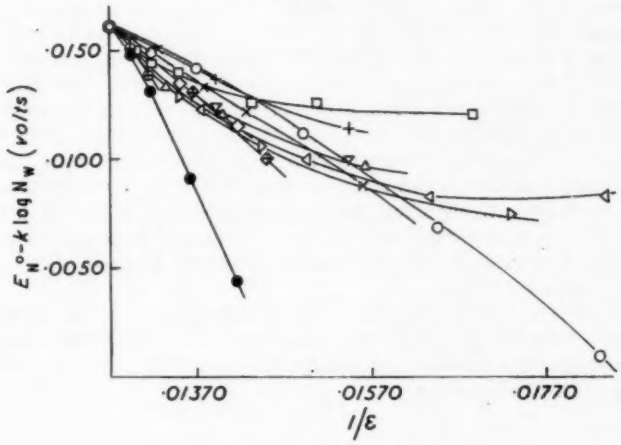


FIG. 4.

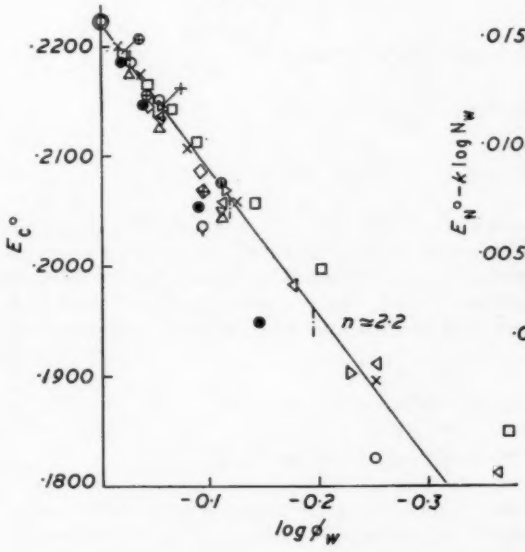
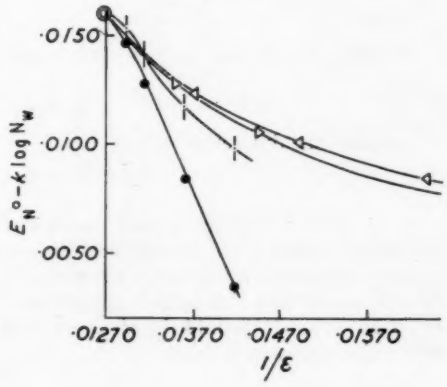


FIG. 5.



[a] $E_N^\circ - k \log N_w$ against $1/\varepsilon$, but with the exception that the monohydric alcohols form a very closely related series of curves, plots of this function do not in general achieve any better correlation between the different solvents (Fig. 3).

Any approach based on the Born equation thus appears to be unsuccessful. A particularly important stumbling block in this treatment is the apparent dependence of

the standard potential for a mixture of given dielectric constant on the nature of the organic component, which is unexpected. A simple approach to the problem of ionic solvation in liquid mixtures has been developed by Hudson and Saville.[6] It is similar to the treatment of concentrated aqueous electrolyte solutions by Robinson and Stokes [7] and by Glueckauf.[8] The position can be put crudely as follows.

The equation for the potential of a charged sphere in a uniform dielectric, on which the Born equation depends, can be expected not to hold particularly well for an ion in solution, since the ion is comparable in dimensions with the solvent molecules. Conditions approaching dielectric saturation then obtain close to the ion. Thus the first layer of solvent molecules around the ion is completely orientated and can be regarded as a firmly bound solvation shell whose formation as the ion enters the solution from the gas phase will be accompanied by a loss of free energy by the co-ordinated water molecules. The remaining free-energy change, which could be computed by an equation of the Born type, is assumed to be comparatively small, especially in solutions of high dielectric constant. Further, in all the solutions considered, the ions are assumed to be preferentially solvated by the more polar molecules, in this case water. This will be particularly true when the water content is high.

Consider the free-energy changes involved in the solution of one mole of hydrogen chloride (as ions) from the gas phase to a standard state in aqueous solution. We can write for the co-ordination of n water molecules (H^+ and Cl^- ions are here written without their charges, and W stands for H_2O) :

$$(H + Cl)_g + nW_{(l)} = (H + Cl), nW$$

For this process

$$\Delta G^{w} = \mu^{w}_{(H+Cl),\,nW} - \mu_{(H+Cl)} - n\mu^{w}_{W}$$

For the same process in an organic solvent–water mixture :

$$\Delta G^{s} = \mu^{s}_{(H+Cl),\,nW} - \mu_{(H+Cl)} - n\mu^{s}_{W}$$

Consider the difference

$$\Delta G = \mu^{s}_{(H+Cl),\,nW} - \mu^{w}_{(H+Cl),\,nW}$$

If we assume that the interaction of the solvated ions with the solvent is negligible, then the difference in the partial molal free energies of the solvated ions in the two solvents depends only on the difference in the concentrations of the solvated ions in the two solvents. We will asume that this term is zero if the standard state is *either* the mole fractional *or* the molar one. It is unlikely of course that the adoption of either scale will make this assumption completely true.

Thus $$\mu^{s}_{(H+Cl)\,nW} = \mu^{w}_{(H+Cl),\,nW}$$

$$\therefore \quad \Delta G^{s} - \Delta G^{w} = n(\mu^{w}_{W} - \mu^{s}_{W}) = -F({}^{s}E^{\circ} - {}^{w}E^{\circ})$$

The partial molal free energy of water in the aqueous mixture can be expressed either in terms of mole-fraction or of volume-fraction statistics. Although the mixtures considered are in practice far from ideal, for the sake of simplicity expressions will be developed for ideal mixtures, whence $\mu^{w}_{W} - \mu^{s}_{W} = -RT \ln N_w$ or $-RT \ln \phi_w$, where ϕ_w is the volume fraction of water.

[6] Hudson and Saville, *J.*, 1955, 4114.
[7] Robinson and Stokes, *J. Amer. Chem. Soc.*, 1948, **70**, 1870.
[8] Glueckauf, *Trans. Faraday Soc.*, 1955, **51**, 1235.

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Thus for the mole-fractional model, using E_N° we have

$$^sE_N^\circ = {}^wE_N^\circ + (RT/F) \ln N_w \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

and for the volume-fractional model, using E_c° we have

$$^sE_c^\circ = {}^wE_c^\circ + (RT/F) \ln \phi_w \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Equation (3) and (4) reduce to

$$^sE_m^\circ = {}^wE_m^\circ + nk \log w + k(n-2) \log (M_{xy}/M_y) \quad . \quad . \quad . \quad (3a)$$

and

$$^sE_m^\circ = {}^wE_m^\circ + nk \log w + k(n-2) \log \rho \quad . \quad . \quad . \quad . \quad (4a)$$

where w is the weight fraction of water, and ρ is the density. In solutions of high water content $\log \rho$ and $\log (M_{xy}/M_y)$ are small, and if n is also close to 2, both expressions approximate to

$$^sE_m^\circ = {}^wE_m^\circ + nk \log w \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Eqn. (5) is a better approximation to (4) than it is to (3) because $\log \rho$ is usually much smaller than $\log (M_{xy}/M_y)$.

Equations (3) and (4) suggest that the plots of E_c° against $\log \phi_w$ and of E_N° against $\log N_w$ should be straight lines from which the solvation number of hydrochloric acid, n, can be determined. The plot of E_N° against $\log N_w$ does not in practice achieve any striking correlation and will not therefore be considered further.

Fig. 4 shows the plot of E_c° against $\log \phi_w$ for all the available systems up to about 50% by volume of water. The correlation achieved is outstandingly better than any found with plots based on the Born equation. In high water concentrations a large number of points lie close to a line for which $n = 2{\cdot}2$, particularly for first members of homologous series. A certain chain-length effect is apparent: at a concentration of about 20% of organic compound the alcohol points lie in order of their molecular weights, and this is also true of the glycols. At higher concentrations, however, the methyl and ethyl alcohol points are reversed in position. It would be of interest to extend the propanol measurements, for example, to higher propanol concentrations. The plot is, however fairly free from marked solvent effects, the only serious deviations being shown by the ethylene glycol, glucose, and dioxan solutions. 5-, 10- and 20-% Acetone solutions obey the stoicheiometric relation closely, but the 40% solution deviates markedly. It is of interest to consider each of these deviations in turn.

Ethylene Glycol.—Ethylene glycol associates in acid solutions. Such association would effectively increase the volume fraction of water in the mixture, so causing E_c° to be higher than expected. The curve is shown to approach the straight line asymptotically at the origin: this is to be expected since the amount of association would decrease with increasing water content.

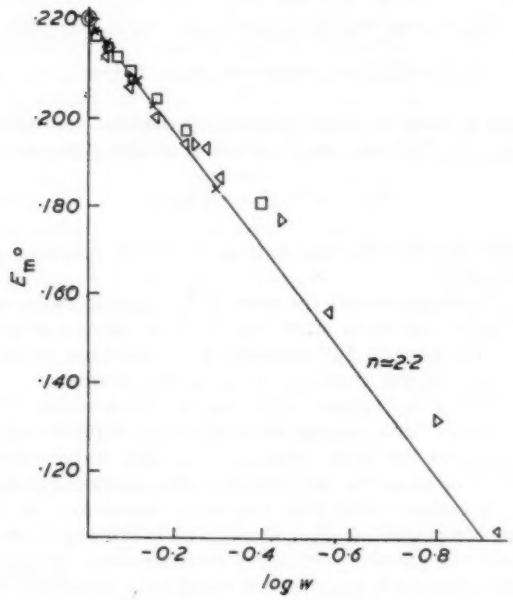
Glucose.—Taylor and Rowlinson [9] have accurately measured vapour pressures of glucose solutions, which show negative deviations from Raoult's law. Scatchard assumed that the similar deviations shown by sucrose solutions are due to hydrate formation, and we have made the same assumption for glucose solutions. It is then possible to calculate a solvation number y by assuming that the activity of water in the solution is proportional to the mole fraction of uncombined water, whence it is easily shown that

$$y = \frac{N_w - a_w}{(1 - N_w)(1 - a_w)}$$

[9] Taylor and Rowlinson, *Trans. Faraday Soc.*, 1955, **51**, 1183.

Table 2 shows the values of y at various glucose concentrations. If these are plotted against the concentration of glucose, the straight line so obtained, on extrapolation to zero concentration, yields $y = 2{\cdot}0$. The four glucose solutions for which e.m.f. measurements are available are comparatively dilute, and y may be taken without great error as 2. On recalculating the volume fraction of water, based on a glucose dihydrate, we find that the results, shown in Fig. 4, are very close to the straight line. The assumption

FIG. 6.



of a glucose dihydrate affects also the calculation of E_N° values, and Fig. 5 shows the plot of $E_N^\circ - k \log N_w$ against $1/\epsilon$ for methyl and ethyl alcohols and glucose. The curve based on the glucose dihydrate shows a marked relation to those of the alcohols. These conclusions are in general agreement with the inference by Taylor and Rowlinson from their thermodynamic measurements that the hydrogen bonding in glucose solutions is stronger than in water.

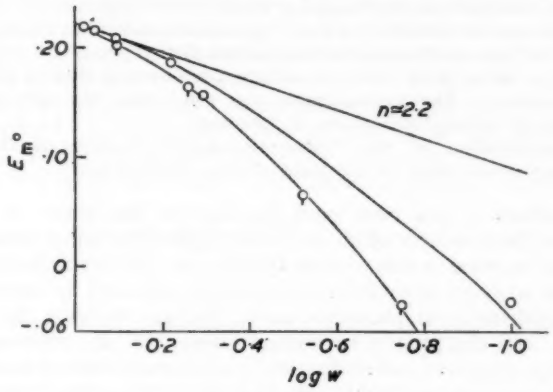
The discussion of the results for glucose solutions indicates that where some correction can be made for non-ideality, the simple stoicheiometric model can be improved. Such corrections may, however, be difficult to make as the vapour-pressure measurements may not be sufficiently sensitive at such low concentrations of organic compound to indicate the extent of change in the effective mole or volume fraction of water.

Acetone and Dioxan.—Fig. 6 shows the plot of E_m° against log w for methyl and ethyl alcohols, glycerol, and ethylene glycol over the range 0—88% of water (v/v). Equation (5) is seen to hold over a wide range for the two alcohols, the only hydroxylic compounds to have been studied over the whole range. By contrast, Fig. 7 shows that acetone and dioxan solutions deviate markedly from the simple stoicheiometric relationship over a wide range, although acetone solutions obey it up to a concentration of 20% acetone (w/w).

The derivation of eqns. (3) and (4) implies an ideal model for the solutions. Hudson and Saville assume in fact that the entropy of water in the solutions considered is ideal,

but stress that this assumption is less likely to be justified when the concentration of either component is small, which is the case for most of the solutions studied here. As mentioned earlier, the partial-vapour-pressure data indicate that the partial molal free energy of water is given by an ideal expression for most of the solutions considered at 25° c. This

FIG. 7.



may, however, be fortuitous, and does not necessarily imply that the entropy of water in the solution will be ideal, or heat-content changes zero or negligible. In ideal solutions the solvation entropy should be given by

$$^{w}_{s}\Delta S = n\boldsymbol{R} \log \phi_w = (\boldsymbol{F}/T)(^{w}E_m^\circ - {}^{s}E_m^\circ)$$

or

$$^{w}_{s}\Delta S = n\boldsymbol{R} \log N_w = (\boldsymbol{F}/T)(^{w}E_N^\circ - {}^{s}E_m^\circ)$$

In fact where entropy data are available from measurements at different temperatures, or from direct heat measurements, they do not follow a simple stoicheiometric expression, and are often in the wrong direction.

The solvation number of hydrochloric acid, $n = 2{\cdot}2$, found from the E_0° *versus* log ϕ_w graph, is lower than that found by any other method, apart from diffusion measurements [10] ($n = 2{\cdot}1$). From consideration of activity coefficients in aqueous solution, Stokes and Robinson find $n = 8$, and Glueckauf $n = 4{\cdot}7$. The E_N° *versus* log N_w graphs give a number of values, all somewhat higher than 2·2 (2·7—5·0).

The values given by Stokes and Robinson and by Glueckauf result from ascribing all the variation of activity coefficient with concentration apart from interionic attractions to specific solvation, and may well be too high on that account. Nevertheless, the present method must not be regarded yet as an entirely reliable method of determining n.

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[10] Robinson and Stokes, "Electrolyte Solutions," Butterworths Scientific Publications, London, 1955, p. 319.

503. *Phospholipids. Part II.* The Stability of Some Derivatives of 2-Aminoethyl Phosphate.*

By D. M. Brown and G. O. Osborne.

Attempts to form 2-aminoethyl dibenzyl phosphate by addition of dibenzyl hydrogen phosphate to ethyleneimine yielded only ethyleneimine polymers. 2-Benzyloxycarboxyamidoethyl diethyl phosphate underwent hydrogenolysis to give a solution containing ethyleneiminium diethyl phosphate, rapid formation of the latter from the intermediate 2-aminoethyl diethyl phosphate being presumed. The mechanism of this conversion, also undergone by 2-aminoethyl diphenyl phosphate, is discussed.

An explanation of the "diazometholysis" reaction of Baer and Maurukas [1] is advanced on the basis of these observations.

Considerable attention has been paid recently to the effect of a neighbouring hydroxyl group on the hydrolysis of di- and tri-alkyl phosphates in relation to nucleic acid chemistry.[2,3] The increase in rate of hydrolysis due to the vicinal function is dependent on a base- or acid-catalysed internal transesterification, followed by rupture of the readily hydrolysed intermediate cyclic phosphate ester. We are studying the effects of other vicinal functions, and the present experiments deal with the amino-group since the 2-aminoethylphosphoryl group and its derivatives are characteristic of many phospholipids. It was hoped, too, to throw some light on the biological action of the "nitrogen mustards," in view of the suggestion [4] that their cytotoxic effects are due *inter alia* to reaction with the phosphate residues of the nucleic acids.

Although Christensen [5] obtained 2-aminoethyl dihydrogen phosphate by interaction of ethyleneimine and syrupy phosphoric acid, we failed to obtain the corresponding dibenzyl ester by using dibenzyl hydrogen phosphate. Materials containing both phosphorus and nitrogen were formed but these were salt-like and appeared to be the dibenzyl phosphates of ethyleneimine and its polymers. Polymerisation of the imine is acid-catalysed,[6] which may partly explain the non-formation of the 2-aminoethyl ester.

As another route, 2-benzyloxycarboxyamidoethanol was phosphorylated with diethyl phosphorochloridate to yield the oily ester (I) which was readily hydrogenated over 10% palladised charcoal to an oil which gave analytical values only approximating to those required for the amine (II) and had none of the expected properties. In particular this product was water-soluble, but insoluble in most organic solvents, and did not yield the expected derivatives when treated with phenyl *iso*thiocyanate or picric acid. On paper chromatography it behaved as an equimolar mixture of ethyleneimine and diethyl hydrogen phosphate and formed polymeric amines on storage. Paper electrophoresis confirmed the salt-like nature of the products. We thus formulate the hydrogenation product as the diethyl phosphate (III) of ethyleneimine and its polymers. In accord with this, passage of its solution through a cation-exchange resin afforded diethyl hydrogen phosphate, which was characterised as the barium salt. We also find that when the hydrobromide of 2-aminoethyl diphenyl phosphate [7] (II; Ph in place of Et) is basified with sodium carbonate, diphenyl hydrogen phosphate is rapidly formed, together with small amounts of phenyl dihydrogen phosphate; from more concentrated solution an oil

* Part I, *J.*, 1957, 2034.

[1] Baer and Maurukas, *J. Biol. Chem.*, 1955, **212**, 39.
[2] Brown and Todd, in "The Nucleic Acids," ed. Chargaff and Davidson, Academic Press, New York, 1955, Vol. I., p. 409.
[3] Brown, Magrath, Neilson, and Todd, *Nature*, 1956, **177**, 1124.
[4] For refs. see Ross, *Adv. Cancer Res.*, 1953, **1**, 397.
[5] Christensen, *J. Biol. Chem.*, 1940, **135**, 399.
[6] Barb, *J.*, 1955, 2564 and refs. therein cited.
[7] Baer and Stancer, *Canad. J. Chem.*, 1956, **34**, 436.

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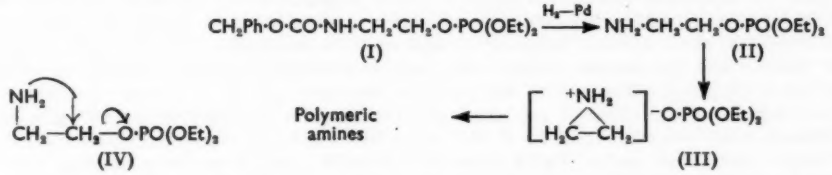
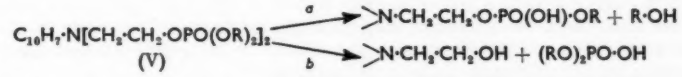
separates which yields on crystallisation the diphenyl hydrogen phosphate of 2-aminoethyl diphenyl phosphate.

Thus it is evident that in systems of type (II), the vicinal amino-group shows no tendency to attack on phosphorus with formation of a cyclic phosphoramidate, but that the preferred reaction depends on attack on carbon with loss of the phosphate anion by alkyl–oxygen fission. Trialkyl phosphates can *N*-alkylate aromatic amines,[8] whereas claims for their conversion into phosphoramidates by aminolysis are of doubtful validity.[9] Formation of the iminium salt (III), presumably *via* the aminoethyl ester (II) by a process of type (IV) has direct analogies, for example in the chemistry of the " nitrogen mustards." These, essentially derivatives of 2-aminoethyl chloride, exist in aqueous solution in equilibrium with the corresponding iminium chloride, concomitant hydrolysis and dimerisation also occurring.[4] The polymerisations encountered in the present work furnish one explanation for the imperceptibility of the back-reaction (III ⟶ II). Moreover Ross and Davis [10] observe that diethyl and diphenyl hydrogen phosphate have very low



" competition factors " for an *N*-aryldi-2-chloroethylamine in comparison with many other anions including monoalkyl phosphates. They also studied the hydrolysis of two compounds (V; R = Et and Ph) by acid and alkali: except in alkaline hydrolysis of (V; R = Ph) where fission at the phenoxy-linkage (*a*) is exclusive, preferential but not exclusive hydrolysis at the aminoethyl linkage (*b*) occurs. Thus the direction of fission (*b*) of these compounds is essentially the same as that of the ester (II) but intrusion of route (*a*) must depend on the low basicity of the arylamino-group and the greater ease of alkaline hydrolysis of phenyl than of alkyl phosphates.[11] We observe that when the



benzyloxycarbonyl derivative (I) is treated with alkali a substance, tentatively identified as 2-aminoethyl ethyl hydrogen phosphate, is formed.

These observations also explain the " diazomethol ysis " reaction of Baer and Maurukas.[1] In this, compounds of the cephalin type (VI; Ac = long-chain acyl residue) where R represents a 2-aminoethyl or *O*-serine, but not a choline, residue are converted by exhaustive treatment with diazomethane, into the corresponding diacylglycerol 1-(dimethyl phosphate) (VII). Methylation will yield a phosphotriester which will break down, as

discussed above, with loss of the residue R as an imine, together, possibly, in the case of (VI; R = serine residue) by β-elimination.[12] Further methylation of the resultant

[8] Thomas, Billman, and Davis, *J. Amer. Chem. Soc.*, 1946, **68**, 895.
[9] See Kosolapoff, " Organophosphorus Compounds," Wiley, New York, 1950, p. 238.
[10] Ross and Davis, *J.*, 1952, 4296.
[11] Plimmer and Burch, *J.*, 1929, 279.
[12] Riley, Turnbull, and Wilson, *Chem. and Ind.*, 1953, 1181.

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monomethyl ester (VI; R = Me) will then yield (VII). Methylation of the cephalin is probably facilitated by partial suppression of zwitterion formation in the non-polar solvent chloroform–ether. 2-Aminoethyl dihydrogen phosphate reacted very incompletely in either suspension with diazomethane, presumably because of the insolubility of the starting material. "Diazometholysis" does not take place when R in (VI) is a choline residue. Since the compound is necessarily zwitterionic it is unlikely that the initial methylation could occur, but, even if it did, break down of the phosphotriester would not occur since the nitrogen atom is already in the quaternary state (cf. the stability of choline diphenyl phosphate [13]).

Experimental

The R_P values quoted in paper chromatographic experiments are for the solvent system butan-1-ol–water (86 : 14) on Whatman No. 1 paper.

2-Benzyloxycarboxyamidoethyl Diethyl Phosphate.—Diethyl phosphorochloridate [14] (3·6 g., 1·1 mol.) in chloroform (5 c.c.) was added to 2-benzyloxycarboxyamidoethanol [15] (3·6 g.) and pyridine (1·85 g., 1·1 mol.) in ice-cold dry carbon tetrachloride (20 c.c.). After 1 hr. the solution was allowed to come to room temperature and set aside overnight. Pyridine hydrochloride was removed and the solution washed with sodium hydrogen carbonate solution and water, then dried (Na_2SO_4). Removal of solvents gave an oily *ester* (5·5 g.) which distilled with decomposition. For analysis it was dried at room temperature for 6 hr. at 10^{-4} mm. over phosphoric oxide (Found: C, 51·2; H, 6·5; N, 4·35. $C_{14}H_{22}O_6NP$ requires C, 50·8; H, 6·7; N, 4·2%). The substance had R_P 0·9 when detected with a phosphate spray reagent.

Hydrogenation of 2-Benzyloxycarboxyamidoethyl Diethyl Phosphate.—The above triester (2·32 g.) was hydrogenated in 4 : 1 aqueous ethanol (40 c.c.) at atmospheric pressure over 10% palladised charcoal (0·43 g.) and palladium oxide (0·1 g.). Hydrogen uptake ceased after 1 hr. (145 c.c. absorbed; theor., 163 c.c. without allowance for evolution of carbon dioxide). After filtration the solvent was removed at reduced pressure below 40°, leaving a pale yellow oil (1·3 g.), soluble in water but insoluble in ether. Its infrared spectrum did not show the characteristic doublet in the 3μ region, associated with a primary amino-group. It gave, on paper chromatography, an elongated spot which was positive to the ninhydrin and the phosphate reagent, with R_P 0·4, whereas trialkyl phosphates have, in general, much higher R_P values.

The oil was submitted to electrophoresis on paper (Whatman No. 4) in ammonium acetate buffers of pH 4·0 and 1·5 with a potential drop of 150 v. In each case a spot positive to the phosphate and negative to the ninhydrin reagent migrated towards the anode at the same rate as an authentic specimen of diethyl hydrogen phosphate. A ninhydrin-positive streak (negative to the phosphate spray) migrated towards the cathode.

On paper chromatography of the oil in sodium hydrogen carbonate solution, the phosphate-positive region had R_P 0·2, corresponding to that of sodium diethyl phosphate, while ninhydrin-positive material occupied a streak, R_P 0·3—0·6. In the same solvent system similar ninhydrin-positive streaks were obtained with partially polymerised ethyleneimine; increasing polymerisation corresponded to increasing R_P value.

An aqueous solution of the oil was percolated through a column (10 × 1 cm.) of Dowex-50 resin (H form). The acidic effluent and aqueous washings were neutralised with barium hydroxide solution, and, after evaporation, the barium salt was precipitated as a colourless amorphous powder by addition of ethanol. Its infrared spectrum was identical with that of barium bis(diethyl phosphate). Paper chromatography in the solvent system propan-2-ol–1% aqueous ammonium sulphate (3 : 2) confirmed the identity.

Elution of the column with dilute aqueous ammonia gave material which corresponded on chromatograms to polymerised ethyleneimine. No further attempt was made to characterise it.

Reaction between Ethyleneimine and Dibenzyl Hydrogen Phosphate.—Ethyleneimine [16] and dibenzyl hydrogen phosphate were brought together in chloroform, water, or without solvent at various temperatures, in proportions varying from ten-fold excess of the imine to a two-fold excess of the acid. Chromatography, as above, showed that only polymerisation of the imine

[13] Baer, *J. Amer. Chem. Soc.*, 1947, **69**, 1253.
[14] Mastin, Norman, and Weilmuenster, *J. Amer. Chem. Soc.*, 1945, **67**, 1662.
[15] Rose, *ibid.*, 1947, **69**, 1384.
[16] Wenker, *ibid.*, 1935, **57**, 2328.

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occurred. Dibenzyl hydrogen phosphate was always recovered when the products were treated with hydrochloric acid.

Action of Diazomethane on 2-Aminoethyl Dihydrogen Phosphate.—A suspension of the phosphate [17] (0·3 g.) was treated overnight with ethereal diazomethane (2 equiv.), then with a further 4 equiv. during two days. Residual undissolved material was removed by filtration. Paper chromatography of the ether solution in the propan-2-ol–1% aqueous ammonium sulphate solvent system revealed the presence of two substances, both positive to the ninhydrin and phosphate spray reagents. The first (R_F 0·42) corresponded to starting material; the second substance was probably 2-aminoethyl methyl hydrogen phosphate since its R_F value, 0·67, was lower than that expected for a triester. A material (positive to ninhydrin and phosphate reagents) with a closely similar R_F value, probably 2-aminoethyl ethyl hydrogen phosphate, was obtained when 2-benzyloxycarboxyamidoethyl diethyl phosphate was heated with sodium hydroxide solution. In neither experiment could we isolate the pure products.

Action of Sodium Carbonate on the Hydrobromide of 2-Aminoethyl Diphenyl Phosphate.—(a) The hydrobromide (240 mg.) in water (10 c.c.) was treated with N-sodium carbonate (2 c.c.). An emulsion was rapidly formed, from which an oil was deposited. This was extracted into ether, the ether solution dried (Na_2SO_4) and evaporated, and the residual oil crystallised from hot ethanol. It formed needles (31 mg.), m. p. 130°. The m. p. was undepressed on admixture with the *diphenyl hydrogen phosphate* of *2-aminoethyl diphenyl phosphate*, an authentic sample of which separated when solutions of the above hydrobromide and excess of sodium diphenyl phosphate were mixed. After recrystallisation from water it had m. p. 130° (Found: C, 56·7; H, 5·0. $C_{26}H_{27}O_6P_2N$ requires C, 57·4; H, 5·0%).

(b) *Chromatography.* When the hydrobromide was heated in a large excess of N-sodium carbonate at 50° for 10 min., paper chromatography in the propan-2-ol–1% ammonium sulphate system showed the presence of diphenyl hydrogen phosphate as the main phosphorus-containing product (R_F 0·85). Monophenyl dihydrogen phosphate (R_F 0·57) was also present together with a trace of a third substance, R_F 0·75, positive both to the phosphorus and the ninhydrin spray reagent. Confirmatory chromatograms were run in butan-1-ol–water (86 : 14).

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[17] Plimmer and Burch, *Biochem. J.*, 1937, **31**, 398.

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504. *Oxygen Heterocycles. Part VIII.* Aroylbenzofurans, Aroyldibenzofurans, and Aroylcoumarins of Potential Biological Interest.*

By NG. PH. BUU-HOÏ, G. SAINT-RUF, T. B. LOC, and NG. D. XUONG.

New 2- and 3-aroylbenzofurans, and 2-aroyldibenzofurans, most of them halogen-containing, have been synthesised, and the Knoevenagel condensation of *o*-hydroxy-aldehydes with aroylacetic esters to give 3-aroylcoumarins has been investigated.

SOME aroylbenzofurans have spasmolytic properties. As they often have also undesirable œstrogenic activity,[1] new 2- and 3-aroylbenzofurans bearing substituents (Cl, Br, alkyl, etc.) known to be unfavourable to œstrogenic activity in the hexœstrol series,[2] have now been synthesised for biological evaluation.

5-Chloro-2-aroylbenzofurans were prepared by Rap–Stoermer condensation[3] of 5-chlorosalicylaldehyde with ω-bromoacetophenones. Phenolic derivatives (I; R = H,

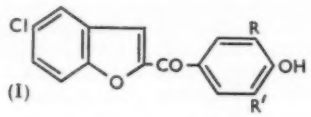
* Part VII, *J.*, 1957, 625.

[1] Bisagni, Buu-Hoï, and Royer, *J.*, 1955, 3693.

[2] Cf. Buu-Hoï, Lavit, and Xuong, *J.*, 1953, 2612; Buu-Hoï, Corre-Hurst, and Xuong, *Bull. Soc. Chim. biol.*, 1955, **37**, 871.

[3] Rap, *Gazzetta*, 1895, **25**, II, 285; Stoermer, *Annalen*, 1900, **312**, 333.

R′ = H, Cl, or Me) were obtained by demethylation with pyridine hydrochloride of the methoxy-ketones similarly prepared from 4-ω-bromoacetylanisoles. Similar condensations and demethylation were performed with 5-bromosalicylaldehyde. Treatment with bromine in acetic acid gave, from 5-chloro-2-*p*-hydroxybenzoylbenzofuran, the dibromo-derivative (I; R = R′ = Br), and from 5-bromo-2-(3-chloro-4-hydroxybenzoyl)benzofuran, a monobromo-derivative.



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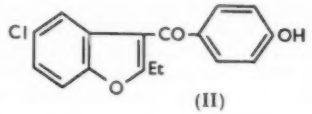

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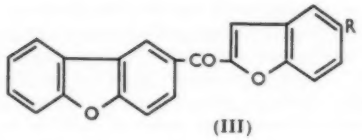

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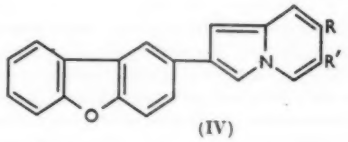

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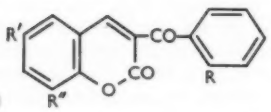

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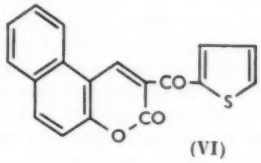

(VI)

5-Chloro-3-aroylbenzofurans were synthesised by Friedel–Crafts acylation of 2-substituted 5-chlorobenzofurans; thus, anisoyl chloride, 5-chloro-2-ethylbenzofuran, and stannic chloride afforded an excellent yield of 3-*p*-anisoyl-5-chloro-2-ethylbenzofuran, which was demethylated to the phenolic ketone (II). Ketones containing both the benzofuran and the dibenzofuran nucleus were synthesised from 2-acetyldibenzofuran,[4] which with bromine in acetic acid yielded 2-bromoacetyldibenzofuran; Rap–Stoermer condensation of the latter with 5-chloro- and 5-bromo-salicylaldehyde afforded 2-(5-chloro-2-benzofuroyl)dibenzofuran (III; R = Cl) and its bromo-analogue (III; R = Br). Other reactions of 2-bromoacetyldibenzofuran included condensation with 2-picoline to an *N*-picolinium salt, which underwent a Tschitschibabin cyclisation [5] in aqueous alkali to 2-2′-dibenzofurylpyrrocoline (IV; R = R′ = H); the 6- and the 7-methyl homologue of the latter were similarly obtained from 2 : 5- and 2 : 4-lutidine.

Several coumarin derivatives have been reported to possess sedative properties,[6] and a number of 3-aroylcoumarins (V) were therefore prepared, by Knoevenagel condensation of ethyl benzoylacetate and ethyl *o*-chlorobenzoylacetate with various *o*-hydroxy-aldehydes in the presence of piperidine. The non-hydroxylated 3-benzoyl- (V; R = H) and 3-*o*-chlorobenzoyl-coumarin (V; R = Cl) were thus prepared. 3-2′-Thenoyl-5 : 6-benzocoumarin (VI) was similarly obtained from 2-hydroxy-1-naphthaldehyde and ethyl 2-thenoylacetate. 3-Acetyl-[7] and 3-benzoyl-7-hydroxycoumarin,[8] were conveniently synthesised by reaction of 2 : 4-dihydroxybenzaldehyde with ethyl acetoacetate and benzoylacetate.

[4] Buu-Hoï and Royer, *Rec. Trav. chim.*, 1948, **67**, 183.
[5] Tschitschibabin, *Ber.*, 1927, **60**, 1607; Buu-Hoï, Jacquignon, Xuong, and Lavit, *J. Org. Chem.*, 1954, **19**, 1370.
[6] von Werder, *Merck's Jahresber.*, 1936, **50**, 88.
[7] Weiss and Merksammer, *Monatsh.*, 1928, **50**, 120.
[8] Ghosal, *J. Indian Chem. Soc.*, 1926, **3**, 108.

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New 3-aroylcoumarins.

Coumarin	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
3-Benzoyl-6-bromo-	177°	$C_{16}H_9O_3Br$	58·1	2·6	58·4	2·7
3-Benzoyl-6-chloro-	163	$C_{16}H_9O_3Cl$	67·2	3·3	67·5	3·2
3-Benzoyl-6 : 8-dichloro-	188	$C_{16}H_8O_3Cl_2$	60·5	2·5	60·2	2·5
3-Benzoyl-8-methoxy-	147	$C_{17}H_{12}O_4$	72·9	4·3	72·8	4·2
3-Benzoyl-6-bromo-8-methoxy-	204	$C_{17}H_{11}O_4Br$	56·6	3·1	56·8	3·1
3-Benzoyl-6-benzyl-	154	$C_{23}H_{16}O_3$	80·9	4·7	81·2	4·7
3-Benzoyl-6-benzyl-8-bromo-	161	$C_{23}H_{15}O_3Br$	66·2	3·7	65·9	3·6
3-*o*-Chlorobenzoyl-6-chloro-	151	$C_{16}H_8O_3Cl_2$	60·5	2·8	60·2	2·5
6 : 8-Dibromo-3-*o*-chlorobenzoyl-	196	$C_{16}H_7O_3Br_2Cl$	43·7	1·4	43·4	1·6
3-*o*-Chlorobenzoyl-6 : 8-di-iodo-	210	$C_{16}H_7O_3I_2Cl$	36·0	1·4	35·8	1·3
3-*o*-Chlorobenzoyl-7-hydroxy- [a]	268	$C_{16}H_9O_4Cl$	63·6	2·9	63·9	3·0

[a] Soluble in aqueous alkalis, to give yellow solutions.

Experimental

2-p-*Bromobenzoyl-5-chlorobenzofuran.*—To a solution of redistilled 5-chlorosalicylaldehyde (10 g.) and potassium hydroxide (3·6 g.) in ethanol (150 c.c.), ω : 4-dibromoacetophenone (18 g.) was added, and the mixture refluxed for 3 hr.; after evaporation of the solvent, water was added, and the *product* collected, and recrystallised twice from ethanol–benzene, giving colourless leaflets (15 g.), m. p. 202° (Found : C, 53·7; H, 2·4. $C_{15}H_8O_2BrCl$ requires C, 53·7; H, 2·4%).

5-Chloro-2-(2 : 4-dimethylbenzoyl)benzofuran.—Similarly prepared from ω-bromo-2 : 4-dimethylacetophenone (10 g.), 5-chlorosalicylaldehyde (6·8 g.), and potassium hydroxide (2·4 g.) in ethanol (120 c.c.), this *ketone* formed prisms (8 g.), m. p. 96°, from ethanol (Found : C, 71·7; H, 4·6. $C_{17}H_{13}O_2Cl$ requires C, 71·7; H, 4·6%).

5-Chloro-2-(p-hydroxybenzoyl)benzofuran (I; R = R′ = H).—The crude methyl ether (10 g.), prepared from 5-chlorosalicylaldehyde (15 g.), ω-bromo-4-acetylanisole (22 g.), and potassium hydroxide (5·3 g.) in ethanol (150 c.c.), was refluxed with redistilled pyridine hydrochloride (15 g.) for 30 min., and water was added after cooling. The precipitate obtained was washed with water, and redissolved in aqueous sodium hydroxide. Acidification with acetic acid afforded a precipitate which recrystallised from aqueous ethanol as prisms (6 g.), m. p. 238° (Found : C, 66·5; H, 3·3. $C_{15}H_9O_3Cl$ requires C, 66·1; H, 3·3%). To a solution of this *ketone* (1 g.) in acetic acid, bromine (1 g., in acetic acid) was added with stirring, and the product poured into water; the precipitate yielded, on recrystallisation from acetic acid, *5-chloro-2-(3 : 5-dibromo-4-hydroxybenzoyl)benzofuran*, prisms (1 g.), m. p. 201° (Found : C, 41·6; H, 1·5. $C_{15}H_7O_3Br_2Cl$ requires C, 41·8; H, 1·6%).

5-Chloro-2-(4-methoxy-3-methylbenzoyl)benzofuran.—This *ketone* (3·8 g.), prepared from ω-bromo-4-methoxy-3-methylacetophenone (6 g.), 5-chlorosalicylaldehyde (4·6 g.), and potassium hydroxide (2 g.), formed prisms, m. p. 128°, from ethanol (Found : C, 68·3; H, 4·5. $C_{17}H_{13}O_3Cl$ requires C, 67·9; H, 4·3%). Demethylation with pyridine hydrochloride (4 g.) yielded *5-chloro-2-(4-hydroxy-3-methylbenzoyl)benzofuran* (I; R = H, R′ = Me), crystallising as needles, m. p. 205°, from aqueous ethanol (Found : C, 67·2; H, 4·1. $C_{16}H_{11}O_3Cl$ requires C, 67·0; H, 3·8%).

5-Chloro-2-(3-chloro-4-hydroxybenzoyl)benzofuran (I; R = H, R′ = Cl).—The crude methyl ether (7 g.), prepared from ω-bromo-3-chloro-4-methoxyacetophenone (11 g.), 5-chlorosalicylaldehyde (11·3 g.), and potassium hydroxide (4 g.), was demethylated by pyridine hydrochloride (10 g.), giving the *hydroxy-ketone* (3 g.), prisms, m. p. 240° (from ethanol–benzene) (Found : C, 58·9; H, 2·7. $C_{15}H_8O_3Cl_2$ requires C, 58·6; H, 2·6%). Bromination of this compound (2·5 g.) with bromine (1 g.) in acetic acid yielded a monosubstitution product.

5-Bromo-2-(3-chloro-4-methoxybenzoyl)benzofuran.—Prepared from 5-bromosalicylaldehyde (11·5 g.; purified by distillation *in vacuo*), ω-bromo-3-chloro-4-methoxyacetophenone (15 g.), and potassium hydroxide (3·2 g.) in ethanol in the usual way, this *ether* formed prisms, m. p. 203°, from ethanol (Found : C, 52·3; H, 2·8. $C_{16}H_{10}O_3BrCl$ requires C, 52·5; H, 2·7%). Demethylation yielded *5-bromo-2-(3-chloro-4-hydroxybenzoyl)benzofuran*, prisms, m. p. 221° (from aqueous ethanol) (Found : C, 50·9; H, 2·4. $C_{15}H_8O_3BrCl$ requires C, 51·2; H, 2·3%); this (2 g.) with bromine (1·2 g.) in acetic acid gave *5-bromo-(5-bromo-3-chloro-4-hydroxybenzoyl)benzofuran* (2·1 g.),

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crystallising as prisms, m. p. 178°, from aqueous ethanol (Found: C, 41·8; H, 1·6. $C_{15}H_7O_3Br_2Cl$ requires C, 41·8; H, 1·6%).

3-p-*Anisoyl*-5-*chloro*-2-*ethylbenzofuran*.—To a water-cooled solution of 5-chloro-2-ethylbenzofuran [9] (12 g.) and *p*-anisoyl chloride (13 g.) in dry carbon disulphide (200 c.c.), stannic chloride (19 g.) was added dropwise with stirring, and the mixture left for 6 hr. at room temperature. After the usual treatment, a *ketone* (12 g.) was obtained which crystallised as leaflets, m. p. 165° from ethanol (Found: C, 68·4; H, 4·6. $C_{18}H_{15}O_3Cl$ requires C, 68·7; H, 4·8%). Demethylation yielded 5-*chloro*-2-*ethyl*-3-p-*hydroxybenzoylbenzofuran* (II), prisms, m. p. 189° (from benzene) (Found: C, 68·0; H, 4·5. $C_{17}H_{13}O_3Cl$ requires C, 67·9; H, 4·3%).

2-*Bromoacetyldibenzofuran*.—2-Acetyldibenzofuran was prepared by Friedel–Crafts acetylation of dibenzofuran according to Buu-Hoï and Royer; [4] bromination of this ketone (11 g.) with bromine (6·9 g.) in acetic acid yielded the *bromo-derivative* (11 g.), which formed needles, m. p. 95°, from methanol (Found: C, 58·0; H, 3·0; Br, 27·5. $C_{14}H_9O_2Br$ requires C, 58·1; H, 3·1; Br, 27·6%).

2-(5-*Chloro*-2-*benzofuroyl*)*dibenzofuran* (III; R = Cl).—A solution of 5-chlorosalicylaldehyde (4·1 g.) and potassium hydroxide (1·5 g.) in ethanol was refluxed for 3 hr. with the foregoing ω-bromo-ketone (8 g.); after evaporation of ethanol and addition of water, the precipitated *product* which formed crystallised as needles (7 g.), m. p. 203°, from ethanol–benzene (Found: C, 72·4; H, 3·1; Cl, 9·9. $C_{21}H_{11}O_3Cl$ requires C, 72·7; H, 3·2; Cl, 10·2%).

2-(5-*Bromo*-2-*benzofuroyl*)*dibenzofuran* (III; R = Br).—Similarly prepared from 5-bromosalicylaldehyde, this *ketone* formed prisms, m. p. 196°, from ethanol–benzene (Found: C, 64·5; H, 3·0. $C_{21}H_{11}O_3Br$ requires C, 64·5; H, 2·8%).

2-2′-*Dibenzofurylpyrrocoline* (IV; R = R′ = H).—A solution of 2-ω-bromoacetyldibenzofuran (2·9 g.) and 2-picoline (2 g.) in ethanol (20 c.c.) was heated at 60° for 1 hr., and ether was added after cooling. The α-picolinium salt, precipitated as prisms, decomp. *ca.* 210°, was dissolved in water (150 c.c.), and the solution boiled for a few minutes with sodium hydrogen carbonate (3 g.); the precipitate which was formed was collected, washed with water, dried, and crystallised from ethanol–benzene, giving sublimable leaflets, m. p. 194—195° (Found: C, 84·8; H, 4·8; N, 4·8. $C_{20}H_{13}ON$ requires C, 84·8; H, 4·6; N, 4·9%). 2-2′-*Dibenzofuryl*-6-*methylpyrrocoline* (IV; R = H, R′ = Me), similarly prepared with 2 : 5-lutidine, formed sublimable leaflets, m. p. 187° (decomp.), from ethanol–benzene (Found: C, 85·2; H, 5·1; N, 4·7. $C_{21}H_{15}ON$ requires C, 84·9; H, 5·1; N, 4·7%). 2-2′-*Dibenzofuryl*-7-*methylpyrrocoline* (IV; R = Me, R′ = H), prepared from 2 : 4-lutidine, formed leaflets, m. p. 203° (decomp.) (Found: C, 85·3; H, 4·9; N, 4·7%).

3-*Benzoyl*-7-*hydroxycoumarin*.—To a mixture of equimolecular amounts of 2 : 4-hydroxybenzaldehyde and ethyl benzoylacetate, a few drops of piperidine (dissolved in ethanol) were added; the solid formed overnight was recrystallised from ethanol, giving colourless needles (85%), m. p. 242° (lit.,[8] m. p. 241°). 3-Acetyl-7-hydroxycoumarin, similarly prepared by use of ethyl acetoacetate, formed needles, m. p. 237°, from ethanol (lit.,[7] m. p. 236°).

Preparation of 3-*Aroylcoumarins* (V).—The aldehydes used were: 5-chloro-, 5-bromo-, 5-benzyl-, 3-benzyl-5-bromo-, 3-methoxy-, 5-bromo-3-methoxy-, 3 : 5-dichloro-, and 3 : 5-dibromo-salicylaldehyde. 5-Bromo-3-methoxysalicylaldehyde, prepared from *o*-vanillin according to Davies,[10] was characterised by its *thiosemicarbazone*, which crystallised as yellowish prisms, m. p. 263—264°, from ethanol–benzene (Found: N, 15·0. $C_9H_{10}O_2N_3SBr$ requires N, 15·4%). The Knoevenagel condensations with ethyl benzoylacetate and ethyl *o*-chlorobenzoylacetate were performed as above, and recrystallisation was from benzene or ethanol–benzene. The *coumarins* thus prepared were sublimable, colourless compounds which readily crystallised.

3-2′-*Thenoyl*-5 : 6-*benzocoumarin* (VI).—Prepared from 2-hydroxy-1-naphthaldehyde (1·7 g.), ethyl 2-thenoylacetate (2 g.), and piperidine (3 drops), this *coumarin* formed yellowish needles (2·8 g.), m. p. 245°, from ethanol (Found: C, 70·5; H, 3·5. $C_{18}H_{10}O_3S$ requires C, 70·6; H, 3·3%).

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The Radium Institute, University of Paris. [*Received, January 24th*, 1957.]

[9] Bisagni, Buu-Hoï, and Royer, *J.*, 1955, 3688.
[10] Davies, *J.*, 1923, **123**, 1579.

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505. *Researches on Acetylenic Compounds. Part LVI.* The Stereochemical Consequences of Some Anionotropic Rearrangements.*

By Ian Bell, E. R. H. Jones, and M. C. Whiting.

In the anionotropic rearrangement of hex-4-en-1-yn-3-ol (" propenylethynylcarbinol ") a mixture of the *cis*- and the *trans*-isomer is formed. Similar results in the allylic replacement of a hydroxyl group by chlorine permit the preparation of *cis*-pent-2-en-4-yn-1-ol.

The rearrangement of hex-4-en-1-yn-3-ol (I) to hex-3-en-5-yn-2-ol (II)[1] has been extensively studied from a mechanistic standpoint.[2] Careful fractionation, however, has now revealed that the product is a mixture of two alcohols with boiling points differing by 10·5°; and spectroscopic evidence proves that these are the *cis*- and the *trans*-isomer of (II). Their formation is not related to stereoisomerism in the starting material, which was found to be homogeneous (and *trans*) by infrared examination of the first and the last fraction after rigorous fractional distillation.

$$\underset{\text{(III)}}{CH_3{\cdot}CHCl{\cdot}CH{=}CH{\cdot}C{\equiv}CH} \xleftarrow{H^+,\,Cl^-} \underset{\text{(I)}}{CH_3{\cdot}CH{=}CH{\cdot}CH(OH){\cdot}C{\equiv}CH} \xrightarrow{H^+,\,H_2O} \underset{\text{(II)}}{CH_3{\cdot}CH(OH){\cdot}CH{=}CH{\cdot}C{\equiv}CH}$$

The heterogeneity of alcohol (II) probably escaped earlier detection through the assumption that the lower-boiling fractions rich in the *cis*-isomer contained unchanged hex-4-en-1-yn-3-ol (I). In fact, the boiling-point of *cis*-(II) is near to that of the unconjugated isomer (I), and each has a refractive index lower than that of *trans*-(II). A mixture of all three isomers cannot conveniently be separated by distillation; a method of isomerisation utilising toluene-*p*-sulphonic acid which provides an (initially) homogeneous reaction mixture is preferable to the earlier steam-distillation technique.[3] The refractive index quoted[3] for hex-3-en-5-yn-2-ol (II) implies a *trans*-content of roughly 80%, whereas the total isomerisation product (yield 85%) is estimated to contain 75—78% of the *trans*-alcohol. On the other hand, the α-naphthylurethane and 3 : 5-dinitrobenzoate[1] were clearly those of the *trans*-isomer; these derivatives of the *cis*-alcohol could not be induced to crystallise. Both isomers gave crystalline *p*-phenylazobenzoates.

When the *cis*-alcohol (II) was treated with 10% aqueous toluene-*p*-sulphonic acid at 35°, as in the isomerisation of (I), it was recovered in good (>75%) yield and shown, by infrared examination, to be free from the *trans*-isomer. Thus the proportions of the two forms are determined by kinetic, rather than thermodynamic, factors.

Treatment of hex-4-en-1-yn-3-ol with concentrated hydrochloric acid gives the corresponding rearranged chloride (III);[4] this also proved to be a mixture of the *cis*- and the *trans*-form (b. p. difference 12°).

Pent-2-en-4-yn-1-ol (IV) was first prepared by the rearrangement-chlorination reaction, followed by hydrolysis[4] (the unconjugated alcohol is rearranged at a negligible rate in the absence of chloride ions[4,2]). Subsequently, and much more conveniently, it was obtained by the action of sodium acetylide on epichlorohydrin.[5] Careful fractionation revealed that when thus prepared, the alcohol contains less than 0·1% of the *cis*-isomer;[6] an unfortunate result, since *cis*-pent-2-en-4-yn-1-ol was a most desirable intermediate, and

$$H_2C{=}CH{\cdot}CH(OH){\cdot}C{\equiv}CH \longrightarrow H_2C{=}CH{\cdot}CHCl{\cdot}C{\equiv}CH + Cl{\cdot}CH_2{\cdot}CH{=}CH{\cdot}C{\equiv}CH \longrightarrow \underset{\text{(IV)}}{HO{\cdot}CH_2CH{=}CH{\cdot}C{\equiv}CH}$$

* Part LV, *J.*, 1957, 2012.

[1] Jones and McCombie, *J.*, 1943, 261.
[2] Braude and his co-workers, *J.*, 1944, 436, 443; 1946, 122, 128, 396; 1947, 1096; 1948, 794, 1982.
[3] Heilbron, Jones, Smith, and Weedon, *J.*, 1946, 54.
[4] Heilbron, Jones, Lacey, McCombie, and Raphael, *J.*, 1945, 77.
[5] Haynes, Heilbron, Jones, and Sondheimer, *J.*, 1947, 1583.
[6] Schlögl, unpublished work.

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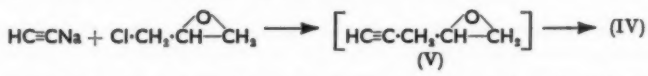
even a 2% content of the *cis*-form would have made this the preferred route. It seems unlikely that the ring-opening of the postulated intermediate (V) would be stereospecific; more probably the *cis*- and the *trans*-form of the alcohol (IV) are both formed, but the former undergoes further reactions (*e.g.*, cyclisation) and is lost.



In a re-examination of the earlier route it was first found that the addition of calcium chloride improved the yield of the chloride mixture from pent-1-en-4-yn-3-ol. In this case fractionation gave not only the *cis*- and the *trans*-conjugated chloride but also some 3-chloropent-1-en-4-yne, readily distinguished by its lack of ultraviolet absorption. The method originally used,[4] *i.e.*, treatment with potassium acetate in methanol, followed by alcoholic potassium hydroxide, proved best for hydrolysing both the conjugated chlorides to the corresponding alcohols. *cis*-Pent-2-en-4-yn-1-ol was finally obtained, after some attention to improving the methods used, in 1·5% overall yield from acraldehyde.

Since the completion of this work Oroshnik [7] has stated that in the rearrangement of 3-methylpent-1-en-4-yn-3-ol *cis*- and *trans*-isomers are formed in comparable quantities, the *cis*-isomer actually predominating. In the three rearrangements discussed above, all leading to a system R·CH=CH·C≡CH as against R·CH=CMe·C≡CH in the case described by Oroshnik, the proportion of *cis*-isomer was constant at 20—25%. The considerable difference between the boiling-points of the stereoisomers of vinylacetylenes (7° for the pent-2-en-4-ynes,[8] as against 0·8° for the penta-1 : 3-dienes) is both interesting theoretically and useful synthetically.

Ultraviolet absorption maxima, all obtained with the same instrument, are tabulated below. The intensity data for the very volatile pent-2-en-4-ynes (rather lower than those reported earlier [8]) are less accurate than those for the other compounds, but the *cis*/*trans* ratio is near unity, in agreement with the earlier results (any error will probably be negative, since the *cis*-isomer is the more volatile). The appreciable reduction in the *cis*/*trans* intensity ratio as the group R in R·CH=CH·C≡CH increases in size cannot in this case imply

Absorption maxima in ethanol of R·CHX·CH=CR′·C≡CH.

			cis	*trans*	
R	X	R′	λ ($10^{-3}\varepsilon$)	λ $10^{-3}\varepsilon$)	$\varepsilon_{cis}/\varepsilon_{trans}$
H	H	H	2215 (11·8)	2225 (12·1)	0·98
H	OH	H	2230 (11·2)	2230 (12·6)	0·89
Me	OH	H	2220 (11·7)	2230 (14·0)	0·84
H	Cl	H	2270 (11·8)	2270 (14·0)	0·84
Me	Cl	H	2255 (12·4)	2265 (15·1)	0·82
H	OH	Me	2230 (11·0)	2240 (13·1)	0·84 [7]

steric hindrance to the coplanarity of the conjugated system, since the *cis*-isomer has a constant intensity of *ca.* 11,500, while those of the *trans*-isomers vary between 12,000 and 15,000. Rather it is the *trans*-form which shows greater sensitivity to hyperconjugative auxochromes, similar to that observed in the diacetylenes,[9] where steric considerations are not relevant. Our results, incidentally, support Oroshnik's assignment of configuration to the isomers of 3-methylpent-2-en-4-yn-1-ol.

In all cases the resolution of vibrational fine structure, though slight, was more perceptible in the *cis*- than in the *trans*-isomers.

The infrared spectra of most of these compounds have already been discussed.[10] The *cis*-compounds R·CH=CH·C≡CH, where R = CH_3, $HO{\cdot}CH_2$, and $ClCH_2$, show a curious anomaly in the intensity of the C–H out-of-plane deformation band, which occurs at

[7] Oroshnik *J. Amer. Chem. Soc.*, 1956, **78**, 2651.
[8] Allan and Whiting, *J.*, 1953, 3314.
[9] Armitage and Whiting, *J.*, 1952, 2005.
[10] Allan, Meakins, and Whiting, *J.*, 1955, 1874.

723, 734, and 768 cm.$^{-1}$, respectively: ε values, under comparable conditions, are 115, 30, and 150, as compared with values of 140, 130, and 150 for the corresponding *trans*-isomers at 956, 952, and 950 cm.$^{-1}$. The weak band of the *cis*-alcohol is abnormally broad; similar results are consistently obtained for other compounds R·CH=CH·C≡C· where R is HO·CH_2 or (to a lesser extent) CH_3·CH(OH).

Experimental

Hex-3-en-5-yn-2-ol (II).—Hex-4-en-1-yn-3-ol (120 g.) was stirred with a solution of toluene-*p*-sulphonic acid (40 g.) in water (400 c.c.) at 35° for 24 hr. The initially homogeneous liquid separated into two phases; the product was isolated with ether and distilled, giving a mixture of isomers (102 g., 85%), b. p. 64—71°/14 mm., n_D^{20} 1·4792—1·4850.

This mixture was distilled at about 18 mm. pressure through a column (50 × 1·4 cm.) packed with 1/16 in. stainless steel rings, a total-condensation still-head set to give a reflux ratio of about 40 : 1 being used. After pre-flooding and heating under reflux for 1 hr., fractions were collected and grouped as follows: (*a*), b. p. 65·5°, n_D^{24} 1·4736—1·4744 (20·6 g.); (*b*), b. p. 65·5—76°, n_D^{24} 1·4772, n_D^{20} 1·4830 (9·7 g.); (*c*), b. p. 76°, n_D^{20} 1·4850—1·4858 (52·5 g.). Fractions (*a*) were the essentially pure *cis*-isomer, and were redistilled through a column (15 × 0·7 cm.) packed with similar rings to give the pure cis-*alcohol*, n_D^{21} 1·4758 (Found: C, 74·75; H, 8·5. C_6H_8O requires C, 74·95; H, 8·4%). Similarly redistilled, the pure *trans*-isomer (*c*) had n_D^{21} 1·4848 (Heilbron, Jones, Smith, and Weedon [3] give b. p. 97—81°/30 mm., $n_D^{18\cdot5}$ 1·4842).

The *cis*-alcohol formed a p-*phenylazobenzoate*, prepared by Mills's method,[11] which formed plates, m. p. 77—78°, from light petroleum (b. p. 40—60°) (Found: C, 75·1; H, 5·35. $C_{19}H_{16}O_2N_2$ requires C, 75·0; H, 5·3%). The same *derivative* of the *trans*-alcohol formed plates, m. p. 99·5—100·5° (Found: C, 75·2; H, 5·15%).

2-*Chlorohex-3-en-5-yne*.—Hex-4-en-1-yn-3-ol (200 g.) and concentrated hydrochloric acid (600 c.c.; *d* 1·16) were shaken mechanically in nitrogen at 18° for 30 min. An equal volume of water was added, and the product was isolated with ether and distilled; it had b. p. 59—70°/70 mm., n_D^{21} 1·4740—1·4858 (202 g., 85%).

The mixture of isomers was fractionally distilled. The column already used for the alcohols was employed with a total-condensation still-head equipped with a magnetically-operated 0·5-c.c. bucket; since a reflux meter permitted measurement of the total boil-up rate, the reflux ratio could be precisely determined. A manostat was used to maintain a pressure of 58—59 mm. After pre-flooding and heating under total reflux for 2 hr. the boil-up and take-off rates were adjusted to 420 and 10 c.c./hr., respectively. The fractions obtained were grouped as follows: (*a*) b. p. 51·8—52·7°, $n_D^{16\cdot5}$ 1·4750—1·4752 (39·8 g.); (*b*) b. p. 52·7—64·0°, $n_D^{16\cdot5}$ 1·4764—1·4862 (22·6 g.); and (*c*) b. p. 64·0°, $n_D^{16\cdot5}$ 1·4868 (9·3 g.). Distillation was then interrupted, the column was washed with a little ether, and the washings and still-residue were distilled through a short Vigreux column to give fraction (*d*), b. p. 63—64°/57 mm., $n_D^{16\cdot5}$ 1·4868—1·4870 (101·4 g.). The pure cis-*isomer* (*a*) had n_D^{20} 1·4732 (Found: C, 62·95; H, 5·85; Cl, 30·9. C_6H_7Cl requires C, 62·9; H, 6·15; Cl, 30·95%); the trans-*isomer* (*c* and *d*; total yield 110·7 g.) had n_D^{21} 1·4850 (Found: C, 63·25; H, 6·1%). Unlike the pent-2-en-4-ynes, the chlorohexenynes did not undergo rapid alteration in air at room temperature, the refractive indices remaining constant during 12 hr; however they did darken slowly, and were best stored at −5° in the presence of quinol.

1-*Chloropent-2-en-4-yne and* 3-*Chloropent-1-en-4-yne*.—Pent-1-en-4-yn-3-ol (125 g.) was added to a solution of anhydrous calcium chloride (167 g.) in concentrated hydrochloric acid (600 c.c.) at 18°, and the mixture was shaken mechanically for 30 min. at 18°. Isolation with ether, removal of the solvent through a 20-cm. Widmer column under partial reflux, and distillation gave the mixed isomers (104 g., 70%), b. p. 70°/82 mm.—79°/40 mm., $n_D^{17\cdot5}$ 1·4510—1·4962.

For fractional distillation the apparatus and technique described for hex-3-en-5-yn-2-ol were employed, with a pressure of 134 mm. The fractions collected may be grouped as follows: (*a*), b. p. 48—50°, n_D^{19} 1·4538 (4·7 g.); (*b*), b. p. 50°, n_D^{19} 1·4570 (14·5 g.); (*c*), b. p. 50—65·5°, n_D^{19} 1·4650—1·4832 (9·4 g.); (*d*), b. p. 65·5°, n_D^{19} 1·4870—1·4874 (13·1 g.); (*e*), b. p. 65·5—75°, n_D^{19} 1·4904 (4·9 g.); (*f*), b. p. 75—76°, n_D^{19} 1·4960—1·4968 (10·3 g.). Distillation of the still residues

[11] Mills, *J.*, 1951, 2332.

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gave additional material (27 g.) (*h*), b. p. 65—67°/89 mm., n_D^{20} 1·4968—1·4972. Of these, fraction (*b*) was 3-chloropent-1-en-4-yne, and after redistillation had n_D^{19} 1·4570 (Found: C, 60·2; H, 5·25. C_5H_5Cl requires C, 59·7; H, 5·0%); fraction (*d*) was cis-1-*chloropent-2-en-4-yne*, and after redistillation had n_D^{19} 1·4870 (Found: C, 59·8; H, 5·05%); and fractions (*f*) and (*h*) were essentially pure trans-1-*chloropent-2-en-4-yne* (Found: C, 59·45; H, 5·1%). The *trans*-chloride contained a trace (*ca.* 1%) of the *cis*-form, according to infrared measurements.

trans-1-*Chloropent-2-en-4-yne* (preparative method; with J. L. H. Allan).—*trans*-Pent-2-en-4-yn-1-ol (10·0 g.) was added dropwise with cooling and stirring to a mixture of pyridine (9·6 g.) and thionyl chloride (21·8 g., 13·1 c.c.) at 0—10°. After being stirred for 18 hr. at 20° the product was poured on ice, and the neutral fraction was isolated with ether. Evaporation of the ether through a 12 in. Fenske column, rapid distillation of the black residue at *ca.* 20°/0·05 mm. into a trap cooled to −80°, and redistillation afforded the *trans*-chloride (6·7 g.), n_D^{19} 1·4982, with an infrared spectrum identical, except for the absence in this case of the band at 768 cm.$^{-1}$ (due to a trace of *cis*-isomer), with that of the specimen described above.

cis-*Pent-2-en-4-yn-1-ol*.—*cis*-1-Chloropent-2-en-4-yne (16·0 g.) was added to a solution of anhydrous potassium acetate (37·5 g.) in methanol (120 c.c.), and the mixture was heated under reflux for 20 hr., potassium chloride separating. Potassium hydroxide (9 g.) was added to the cooled mixture which was stirred to effect solution. After 24 hr. at 20° ether was added and the precipitate was filtered off and washed with ether; the resultant solution was carefully made neutral (phenolphthalein) by addition of *ca.* 2 c.c. of 10% phosphoric acid. The ethereal solution was dried thoroughly ($MgSO_4$), then concentrated through a 20-cm. Widmer column under partial reflux. Distillation of the residue gave cis-*pent-2-en-4-yl-1-ol* (5·85 g.), b. p. 68—69°/19 mm., $n_D^{20\cdot5}$ 1·4870—1·4880. An analytical specimen had $n_D^{21\cdot5}$ 1·4882 (Found: C, 72·7; H, 7·4. C_5H_6O requires C, 73·15; H, 7·35%). It could be kept for months at −18° to −40°, and indeed seemed more stable than the *trans*-isomer. The p-*phenylazobenzoate* formed plates, m. p. 83·5—84·5°, from light petroleum (b. p. 40—60°) (Found: C, 74·55; H, 5·05. $C_{18}H_{14}O_2N_2$ requires C, 74·5; H, 4·85%). The same *derivative* of the *trans*-alcohol had m. p. 102—103° (Found: C, 74·3; H, 4·8%).

We are indebted to the Ministry of Education for a State Scholarship to one of us. We thank Mr. E. S. Morton and his colleagues for microanalyses. Infrared spectra were determined under the supervision of Dr. G. D. Meakins and Dr. F. B. Strauss.

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The University, Manchester, 13. [*Received, February 7th*, 1957.]

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506. *Structural Chemistry of the Alkoxides. Part IX.* tert.-Alkoxides of Quadrivalent Cerium.*

By D. C. Bradley, A. K. Chatterjee, and W. Wardlaw.

Ceric *tert.*-alkoxides $Ce(OR)_4$, where R = CMe_3, CMe_2Et, $CMeEt_2$, CEt_3, CMe_2Pr^n, CMe_2Pr^i, and $CMeEtPr^n$, have been prepared from $Ce(OPr^i)_4.Pr^iOH$ by alcohol interchange, and their molecular weights have been determined ebullioscopically in benzene and in toluene. The higher *tert.*-alkoxides are the first volatile liquid compounds of cerium(IV) to be reported and their boiling points under reduced pressure were determined. The results are discussed in terms of the stereochemical theory for the Group IVA metal alkoxides.

Recently we established that the molecular complexities of primary [1] and secondary [2] alkoxides of quadrivalent cerium were significantly lower than those of the corresponding derivatives of thorium. These results were surprising in view of the supposed equality in atomic radii of cerium and thorium and it was suggested that electronic factors rather than steric factors might be responsible for this contrast. We have now prepared a number

* Part VIII, *J.*, 1956, 4439.

[1] Bradley, Chatterjee, and Wardlaw, *J.*, 1956, 2260.
[2] *Idem*, *J.*, 1956, 3469.

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of *tert.*-alkoxides of cerium because it was expected that the higher *tert.*-alkoxides would be monomeric and less susceptible to electronic factors owing to the screening effect of the large *tert.*-alkoxide groups. Moreover, there was the added interest of determining whether stable monomeric compounds of quadrivalent cerium existed because the stability of the primary and secondary alkoxides might be ascribed to their complex nature.

Attempts to prepare *tert.*-alkoxides of cerium by the "ammonia method" on dipyridinium cerium hexachloride gave the monochloride tri-*tert.*-alkoxide complexes $CeCl(OR)_3,C_5H_5N$, where R = CMe_3 or CMe_2Et, and in this respect cerium resembles zirconium [3] which likewise gave the monochloride complex $ZrCl(OCMe_3)_3,2C_5H_5N$. The corresponding reaction for thorium has not yet been investigated but earlier work [4] on $(C_5H_6N)_2ThCl_6$ showed that some chlorine remained in the product when ethanol or propan-2-ol was used, in contrast to the behaviour of zirconium and cerium which gave tetra-alkoxides with primary and secondary alcohols. The new cerium tetra-*tert.*-alkoxides $Ce(OR)_4$, where R = CMe_3, CMe_2Et, $CMeEt_2$, CEt_3, CMe_2Pr^n, CMe_2Pr^i, and $CMeEtPr^n$, were prepared from cerium *iso*propoxide by alcohol interchange. All of these compounds are extremely sensitive to water but otherwise are stable. The *tert.*-butoxide and the *tert.*-amyloxide were deep yellow solids which sublimed unchanged in a "molecular still" whilst the higher *tert.*-alkoxides were bright yellow liquids which were distilled unchanged under reduced pressure. The boiling points and the molecular weights determined ebullioscopically in benzene and in toluene are recorded in Table 1 together with the molecular complexities. These are the first recorded examples of volatile liquid compounds of quadrivalent cerium and establish conclusively their stability. In fact our preliminary studies on tervalent cerium alkoxides show that the latter are relatively unstable since they are readily oxidised by traces of atmospheric oxygen to the ceric state. In view of the striking increase in stability from $CeCl_4$ to $[CeCl_6]^{2-}$ it seemed possible that the stability of the ceric primary [1] and secondary [2] alkoxides might be due to their complex nature. However, the data in Table 1 show that monomeric ceric alkoxides are also stable although it is possible that in these compounds stability is achieved by intramolecular covalency expansion, *viz.*, $^-Ce{=}O^+{-}R$. On the other hand this double bonding would lower the thermal stability in a *tert.*-alkoxide by promoting the release of a carbonium ion (cf. niobium alkoxides [5]), but in fact the ceric derivatives of 2-methylpentan-2-ol and 2 : 3-dimethylbutan-2-ol are more stable than the corresponding thorium derivatives [6] which decompose above 120° *in vacuo*.

The results in Table 1 show that the molecular complexity and volatility of ceric *tert.*-alkoxides are much more dependent on size and shape of the alkyl group than was

TABLE 1.

R in $Ce(OR)_4$	B. p./mm.	In benzene		In toluene	
		Mol. wt.	Complexity	Mol. wt.	Complexity
CMe_3	140—150°/0·1 *	1062	2·5	968	2·2
CMe_2Et	240°/0·1 *	1150	2·4	1050	2·2
$CMeEt_2$	140°/0·06	746·2	1·4	580·4	1·1
CMe_2Pr^n	146°/0·05	761·7	1·4	600	1·1
CMe_2Pr^i	132°/0·05	584	1·1	541·6	1·0
CEt_3	154°/0·05	650·3	1·1	604·7	1·0
$CMeEtPr^n$	150°/0·05	604·5	1·0	—	—

* Sublimation.

found with the primary or secondary alkoxides, and this is consistent with the stereochemical theory already advanced to account for the physicochemical properties of Group IVA metal alkoxides. The lower complexities found in toluene confirm the depolymerising effect of the higher-boiling solvent as already noted for the primary and secondary

[3] Bradley, Halim, Sadek, and Wardlaw, *J.*, 1952, 2032.
[4] Bradley, Saad, and Wardlaw, *J.*, 1954, 1091.
[5] Bradley, Chakravarti, and Wardlaw, *J.*, 1956, 2381.
[6] Bradley, Saad, and Wardlaw, *J.*, 1954, 3488.

alkoxides. A remarkable feature of the ebullioscopic measurements on metal alkoxides [1, 2, 5, 7] is the clear effect of temperature in dissociating the complex molecules in contrast to the absence of concentration effects within the range of concentrations studied. Unfortunately this prevents the calculation of dissociation constants or heats of dissociation for the complex alkoxides, and these would provide fundamentally sounder parameters for comparison than the molecular complexities.

The present results allow a very interesting comparison between tertiary alkoxides of titanium, zirconium, cerium(IV), and thorium. The boiling points (corrected to 0·1 mm.) and molecular complexities in benzene (in parentheses) are shown in Table 2 for a number

TABLE 2.

R in $M(OR)_4$	Ti	Zr	Ce	Th
CMe_3	52 (1·0)	50 (1·0)	150 (2·4)	160 (3·4)
CMe_2Et	98 (1·0)	95 (1·0)	240 (2·3)	198 (2·8)
$CMeEt_2$	128 (1·0)	128 (1·0)	145 (1·4)	148 (1·8)
CMe_2Pr^n	144 (1·0)	137 (1·0)	152 (1·4)	Dec.* (2·6)
CMe_2Pr^i	153 (1·0)	133 (1·0)	138 (1·1)	Dec.* (2·3)
CEt_3	166 (1·0)	166 (1·0)	160 (1·1)	154 (1·0)
$CMeEtPr^n$	—	—	156 (1·0)	153 (1·7)

* Decomp. at 120°/0·1 mm.

of derivatives. These results reinforce the argument deduced from the behaviour of primary and secondary alkoxides that on the basis of stereochemical effects alone the atomic radii should be in the order Th > Ce > Zr > Ti. Thus the lower tertiary alkoxides of cerium are significantly less polymerised than the corresponding thorium derivatives. It is also clear that differences in ionic character of the metal–oxygen bonds cannot be very important because in the monomeric series of triethylcarbinol derivatives the boiling points are all within a few degrees of 160°. In fact the order of boiling points Zr > Ce > Th is exactly the reverse of that predicted from the order of ionic character Th > Ce > Zr required to explain the variation in molecular complexities of the lower tertiary alkoxides of these elements. On the other hand, the order of volatilities is not surprising in terms of the theory of the fundamental effect of mass on volatility [8] which suggests that in a series of compounds with similar molecular sizes and latent heats of vaporisation the heavier molecules may be the more volatile. Since we were dealing with essentially covalent compounds we have previously taken the covalent atomic radii given by Sidgwick [9] for comparative purposes (*i.e.*, $r_{Ce} = r_{Th} = 1{\cdot}65$ Å). Similarly Moeller [10] gives values of $r_{Ce} = 1{\cdot}646$ Å and $r_{Th} = 1{\cdot}652$ Å. On the other hand Goldschmidt's [11] ionic radii for co-ordination number 6 are Ce^{4+} 1·02 Å, $Th^{4+} = 1{\cdot}10$ Å, *i.e.*, in the order required from our studies on the alkoxides. Now according to Moeller [10] the covalent radii of these elements were deduced from interatomic distances in the metals and this should give comparable radii for metals of the same Group valency. However, although ceric cerium has a formal analogy to the Group IVA elements, yet in the cerous state it is also a member of the lanthanon series of tervalent metals. We suggest that the "covalent" radius of 1·65 Å assigned to cerium is not appropriate to this element in the quadricovalent state but suggest instead a value of 1·55—1·60 Å. This is supported by the fact that the value of 1·65 Å for cerium falls reasonably on a plot of covalent radius against atomic number from La = 1·69 Å to Sm = 1·64 Å, as expected for a tervalent metal and in contrast to the sudden reduction in radius from lutetium (1·56 Å) which is tervalent to hafnium (1·44 Å) which is quadrivalent. Moreover, europium (covalent radius 1·85 Å) is strikingly off this curve and has a value more appropriate to a bivalent metal (cf. Ba = 1·98 Å) and this accords with its well-known bivalency. Similarly the tervalent

[7] Bradley, Wardlaw, and Whitley, *J.*, 1956, 5.
[8] Bradley, *Nature*, 1954, **174**, 323.
[9] Sidgwick, "The Chemical Elements and Their Compounds," Oxford, 1950, Vol. I, p. xxix.
[10] Moeller, "Inorganic Chemistry," Wiley, New York, 1952, p. 135.
[11] Goldschmidt, *Ber.*, 1927, **60**, 1263.

ionic radii of Ce^{3+} (1·18 Å) and Eu^{3+} (1·13 Å) both fall on the smooth plot of r_M^{3+} against atomic number for the lanthanons, whereas the value for Ce^{4+} is noticeably off it (see also Pr^{4+} 1·00 Å). We therefore conclude that the quadricovalent radius of cerium is less than that of thorium, in accordance with our deductions from the stereochemical behaviour of the tetra-alkoxides of the Group IVA elements.

Experimental

The experimental details of this work were similar to those previously described.[1,2]

The Complex, $CeCl(OBu^t)_3,C_5H_5N$.—The complex chloride (4·5 g.) was suspended in *tert.*-butyl alcohol–benzene azeotrope (300 c.c.). Ammonia was passed into the suspension until it had cooled to room temperature. After the removal of excess of ammonia under reduced pressure and ammonium chloride by filtration, the filtrate was evaporated under reduced pressure to about half its original volume. The lemon-yellow crystalline *product* (12 g.) was filtered off and dried at 40°/0·1 mm. [Found: Ce, 29·7; Cl, 7·5. $CeCl(OC_4H_9)_3,C_5H_5N$ requires Ce, 29·6; Cl, 7·5%]. Even prolonged treatment of the foregoing product with ammonia and alcohol failed to replace the chlorine in the cerium complex.

The Complex, $CeCl(OCMe_2Et)_3,C_5H_5N$.—The complex cerium chloride (44 g.) was suspended in a mixture of *tert.*-amyl alcohol (100 c.c.) and benzene (350 c.c.), and ammonia was passed into it for long after the products had cooled to room temperature. From the filtered solution evaporated to half bulk was obtained a bright yellow crystalline *product* (15 g.) which was filtered off and dried at 40°/0·1 mm. [Found: Ce, 27·3; Cl, 6·9. $CeCl(OC_5H_{11})_3,C_5H_5N$ requires Ce, 27·2; Cl, 6·9%].

Cerium Tetra-tert.-*butoxide*.—The benzene–*tert.*-butyl alcohol azeotrope (400 c.c.) and the recrystallised complex *iso*propoxide (6·15 g.) were refluxed for about 12 hr. The distillate was then collected first very slowly and then rather rapidly, until 50 c.c. of the liquid remained. To this were added another (450 c.c.) of *tert.*-butyl alcohol–benzene azeotrope. The azeotropic distillation was repeated and most of the solvent was distilled off; on cooling, yellow needles (5·8 g.) separated and were dried at 70°/0·1 mm. [Found: Ce, 32·4. $Ce(OC_4H_9)_4$ requires Ce, 32·4%].

The Higher Alkoxides.—The tetra-*tert.*-amyloxide and all other higher alkoxides were prepared by alcohol interchange involving ceric *iso*propoxide and the alcohol in benzene. Some typical results are in Table 3.

Table 3.

R	ROH taken (g.)	$Ce(OPr^i)_4$,Pr^iOH taken (g.)	C_6H_6 (c.c.)	Yield of $Ce(OR)_4$ (g.)	Ce (%) Found	Ce (%) Reqd.
CMe_2Et	13·5	3·7	100	3·1 [a]	28·8	28·7
$CMeEt_2$	50	8·5	200	8·2 [b]	25·7	25·7
CMe_2Pr^n	27·7	4·8	120	4·5 [b]	25·6	25·7
CMe_2Pr^i	24	7	150	4·8 [b]	25·7	25·7
CEt_3	30·1	20	150	24 [b]	23·3	23·3
$CMeEtPr^n$ ...	48·4	5·1	110	6·2 [b]	23·4	23·3

[a] Yellow solid. [b] Mobile liquid.

Table 4.

R in $Ce(OR)_4$	Range of m(g.)	Wt. of C_6H_6 (g.)	$\Delta T/m$ (°c/g.)	Mol. wt. Found	Mol. wt. Calc.
CMe_3	0·0376—0·2484	16·06	0·1765	1041	432·1
CMe_2Et	0·0247—0·2592	16·34	0·1570	1150	488·1
$CMeEt_2$	0·0586—0·1718	15·03	0·3360	584	544·1
CMe_2Pr^n	0·0252—0·3760	14·54	0·2710	749	544·1
CMe_2Pr^i	0·0249—0·3542	15·24	0·2542	761·7	544·1
CEt_3	0·0404—0·3077	15·93	0·2838	650·3	600·1
$CMeEtPr^n$	0·1502—0·2405	16·26	0·2982	604·5	600·1

Molecular-weight Determinations.—All determinations involving the use of the apparatus constant (found with azobenzene) were checked by the internal calibration technique using fluorene.[1,2] Typical results for the first method (in benzene) are given in Table 4 and for the internal calibration method (in toluene) in Table 5.

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TABLE 5.

R in $Ce(OR)_4$	Alkoxide Range of m(g.)	Alkoxide $\Delta T/m$ (mm./g.) *	Fluorene Range of m(g.)	Fluorene $\Delta T/M$ (mm./g.) *	Mol. wt. Found	Mol. wt. Calc.
CMe_3	0·0211—0·1360	130	0·0080—0·0516	749	958	432·1
CMe_2Et	0·0251—0·1452	117·4	0·0068—0·0459	742	1050	488·1
$CMeEt_2$	0·0298—0·1390	232·5	0·0150—0·0378	739	541·6	544·1
CMe_2Pr^n	0·0114—0·1130	210	0·0265—0·0540	757·1	600	544·1
CMe_2Pr^i	0·0097—0·0935	200	0·0034—0·0314	679	564·2	544·1
CEt_3	0·0295—0·1377	244	0·0079—0·0453	882·1	601	600·1

* ΔT in terms of mm. of water pressure.

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507. *The Exchange of Oxygen between Alcohols and Water. Part III.*[1] *Acid-catalysed Racemization and Oxygen Exchange of 1-Phenylethyl Alcohol in Dilute Aqueous Solutions.*

By ERNEST GRUNWALD, ADAM HELLER, and F. S. KLEIN.

For 1-phenylethyl alcohol in dilute aqueous perchloric acid, the ratio of the acid-catalysed rates of oxygen exchange to racemization, after correction for olefin formation, is 0·82 ± 0·04. The ratio is less than unity owing to the shielding by the departing $^-OH_2$ group. A simplified model was developed for the quantitative interpretation of this shielding, use of which, with stereochemical data for 1-phenylethyl chloride, showed that OH_2 and Cl^- are equally effective at shielding. The results suggest that the rate of dissociation of the solvated $R^+ \cdots X$ intermediate (which is the first product in the ionization of RX) to a free carbonium ion is slow compared with its rate of substitution with the solvent.

In aqueous perchloric acid, the salt-effect on the specific rate of racemization of 1-phenylethyl alcohol was intermediate between that expected from the H_0 and the C_0 function.

PREVIOUS kinetic studies of the acid-catalysed oxygen exchange between water and alcohols[1,2] are now extended to the 1-phenylethyl system. Specific rates (k_{exch}) measured in dilute aqueous solution are compared with rates of racemization of optically active alcohol (k_{rac}) and of olefin formation (k_{ol}) under the same conditions. From the measured values of $k_{exch}/(k_{rac} - k_{ol})$, the steric course of the substitution has been deduced. The results supplement studies in the *sec.*-butyl system[3] and provide significant information about the solvation and the reactions of the carbonium-ion intermediates.

EXPERIMENTAL

Materials.—Optically active 1-phenylethyl alcohol, prepared *via* the brucine salt of the phenylethyl hydrogen phthalate by known methods,[4,5,6] had b. p. 91—91·5°/(~10 mm.); m. p. 9—11°; n_D^{24} 1·5258; $[\alpha]_D^{24}$ of the pure alcohol [from (−)-brucine salt] +54·3°; in ethanol,

[1] Part II, Dostrovsky and Klein, *J.*, 1955, 4401.
[2] Dostrovsky and Klein, *J.*, 1955, 791.
[3] Bunton, Konasiewicz, and Llewellyn, *J.*, 1955, 604.
[4] Kenyon and Houssa, *J.*, 1930, 2260.
[5] Downer and Kenyon, *J.*, 1939, 1156.
[6] Ott, *Ber.*, 1928, **61**, 2139.

$-35{\cdot}2°$ ($c = 1{\cdot}58$); in water, $-27{\cdot}8°$ ($c = 0{\cdot}96$). The (−)-alcohol was of lower optical purity, $[\alpha]_D^{24}$ 28·8°.

(±)-1-Phenylethyl alcohol was obtained pure from the hydrolysis of twice-recrystallized 1-phenylethyl hydrogen phthalate (m. p. 107·5—108·5°) in boiling 5N-sodium hydroxide (10 min.). The alcohol was extracted with pure ether, dried (K_2CO_3), and distilled at 3—4 mm. It had m. p. 19—20°.

Good commercial styrene which had been stored at −20° was distilled at a pressure less than 1 mm. The styrene obtained had a bromine number of 149 ± 5, corresponding to 97 ± 3% purity, and $n_D^{21{\cdot}7}$ 1·5452.

Isotopically enriched water from the ^{18}O-production plant of the Weizmann Institute was redistilled from alkaline permanganate. Perchloric and hydrochloric acid were of Reagent Grade and were standardized with aqueous sodium hydroxide; potassium hydrogen phthalate obtained from the U.S. National Bureau of Standards served as primary acidimetric standard. Hydrochloric acid was the constant-boiling azeotrope.[7]

Analysis of ^{18}O *in 1-Phenylethyl Alcohol.*—70 ml. samples of 0·08M-alcohol in aqueous perchloric acid were added to sufficient reagent-grade potassium carbonate to give saturated solutions. These were extracted, first with 20 ml., and then three times with 10 ml. of pure ether. The ether extracts were dried (K_2CO_3) and most of the ether was evaporated. The residue of alcohol and a little ether was dried carefully by shaking overnight with 80—100-mesh potassium carbonate, a treatment which removed the last detectable traces of water. The mixture was then centrifuged, and the liquid withdrawn by means of a syringe, and distilled through an efficient micro-column at a pressure of about 1 mm. After complete removal of the ether, successive 150 mg. fractions of distillate were collected, and from each fraction 122 mg. (1 mmole of alcohol) were withdrawn with a calibrated micropipette and analysed [8] for ^{18}O. The only modification of this method [8] used here was to heat the alcohol–CO_2–H_2SO_4 mixtures at 150° for 24 hr., instead of at 170° for 3 hr. This gave better precision and was shown to give isotopic equilibrium between carbon dioxide and the ^{18}O of the alcohol. (Heating for 48 hr. at 150° gave identical results.) The isotopic composition of successive fractions of distillate, determined by this method, proved to be equal to better than ±0·003 atom-% of ^{18}O.

Polarimetry.—Optical rotations were measured by means of a polarimeter (O. C. Rudolph and Sons), using a 2 dm. microtube of 2 ml. volume. The light source was an intense sodium-vapour lamp, with a filter to isolate the sodium D doublet. The mean deviation of single readings varied with the angle between the Nicol prisms of the polarizer in the following way: 1°, ±0·002°; 2°, ±0·003°; 3°, ±0·004°; 4°, ±0·004°; 5°, ±0·005°; 7°, ±0·008; angles in the range 3—4·5° were used in the rate measurements. The precision was considerably worse with a less intense light source which required a larger angle between the Nicol prisms.[9]

For good precision, care was taken to keep the position of the polarimeter tube always the same and to avoid errors due to anisotropy in the cover glasses, due to pressure, by reading the tube from both sides, and by avoiding strong pressure on them. The mean of about 10 readings was taken for each point. The measured rotations were shown to be proportional (±0·002°) to the fraction of active alcohol in the rate-measurements by use of aqueous solutions of active and (±)-alcohol.

Ultraviolet Spectrophotometry.—Concentrations of styrene in the presence of 1-phenylethyl alcohol were measured by means of a Beckman DU spectrophotometer at 2300 and 2450 Å. The molar extinction coefficients were: for styrene, 7900 ± 400 at 2450 Å and 4300 ± 200 at 2300 Å; for 1-phenylethyl alcohol, 82 at 2450 and 20·3 at 2300 Å. The values for the alcohol may be too high because of the difficulty of removing all traces of styrene.

Kinetic Measurements.—Precise measurements of k_{exch} and k_{rac} were possible in spite of the low water solubility of the alcohol (0·12M at 20°) [10] and the even lower water solubility ($2—6 \times 10^{-4}$M) of the styrene [11] produced in the simultaneous elimination reaction. The latter reaction was fortunately very slow, and by using an alcohol preparation which contained initially only a trace of styrene, the reactions could be followed to nearly two half-lives without the appearance of a second phase.

[7] Foulk and Hollingsworth, *J. Amer. Chem. Soc.*, 1923, **45**, 1220.
[8] Anbar, Dostrovsky, Klein, and Samuel, *J.*, 1955, 155.
[9] W. Heller, in "Physical Methods of Organic Chemistry," ed. Weissberger, Interscience Publ., New York, 1949.
[10] Hjort and Kaufmann, *J. pharm. exp. Therap.*, 1920, **15**, 130.
[11] Boundy and Boyer, "Styrene," Reinhold Publishing Corp., New York, 1952.

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Samples of kinetic results are shown in Table 1; α is the observed optical rotation, and N the atom fraction of ^{18}O of the alcohol. N_W is the essentially constant atom fraction of ^{18}O of the water in the medium. Both k_{exch} and k_{rac} are listed as *second-order* rate constants, *i.e.*,

$$k_{exch} = \ln [(N_W - N_0)/(N_W - N_t)]/t[H^+] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$k_{rac} = \ln (\alpha_0/\alpha_t)/t[H^+] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$[H^+]$ is constant in each run. Within experimental error, the data were fitted well by equation (1) or (2) in any given run, and average rate constants were computed by standard least-squares methods. On the basis of the precision of the raw results and of the reproducibility of several duplicate runs, the standard error of the rate constants was estimated as 2% for k_{exch} and 4% for all comparable values of k_{rac}. These figures apply to all results in perchloric acid except

TABLE 1. *Sample of kinetic results at* 30·4°. Concn. of alcohol, 0·0845M; $HClO_4$, 0·01721N; water enriched in ^{18}O.

Racemization			Exchange		
t (hr.)	α	$10^5 k_{rac}$ (sec.$^{-1}$ mole^{-1} l.)	t (hr.)	100 N †	$10^5 k_{exch}$ (sec.$^{-1}$ mole^{-1} l.)
0·0	0·573°	—	0·0	0·204	—
117·8	0·519	1·35	94·5	0·309	1·04
242·5	0·473	1·28	170·0	0·388	1·03
384·3	0·430	1·21	268·3	0·488	1·05
450·6	0·405	1·24	360·9	0·582	1·07
597·3	0·355	1·30	500·6	0·696	1·03
∞	0·000 ± 0·002 *			N_W 1·985 ± 0·03	

* From results at higher temperatures.
† Value after dilution with 6 moles % of normal CO_2.

those in 0·5N- and 1N-acid, or in hydrochloric and hydrobromic acids. In the exceptional cases, values of α_0 were, for practical reasons, kept rather small, and the accuracy of k_{rac} was only about ±10%.

Two comments are necessary regarding the values of k_{exch}. First, it is possible that some of the exchange occurs *via* the rehydration of the styrene produced in the simultaneous elimination reaction, rather than by a substitution mechanism. In order to check this, the rate constant (k_H) for the acid-catalysed hydration of styrene was measured separately (see below). Using the measured values of k_{ol} and k_H, we found that the correction to k_{exch} due to this cause was less than 0·1% in all experiments, so it was neglected. Secondly, one would like to know the magnitude of the kinetic isotope effect involved in k_{exch} before comparing k_{exch} and k_{rac}. Since ^{18}O was *introduced* into the alcohol, and since eqn. (1) contains N_W rather than N_∞, it can be shown [12] that k_{exch} is, in effect, the rate constant for the reaction of $R^{16}OH$ with $H_2{}^{18}O$. For an S_N1 mechanism in which the rate-determining step involves the rupture of the R–O bond, the rate of this reaction must be very nearly equal to that of the reaction of $R^{16}OH$ with $H_2{}^{16}O$. Kinetic isotope effects are therefore negligible in the rate comparisons to be made in this paper.

All runs were made in thermostats of conventional design. Temperatures were constant to 0·05° and were measured with a thermometer calibrated by the National Physical Laboratory. In the measurements at 30·4°, the reaction mixtures were kept in glass-stoppered volumetric flasks well immersed in the thermostat. In all other measurements, sealed ampoules were used. At suitable intervals the reactions were quenched by shaking the ampoules in crushed ice, and the reaction mixtures analysed at once.

Hydration–Dehydration Rate Measurements.—The rate-constants for the acid-catalysed elimination reaction, k_{ol}, and for the acid-catalysed hydration of styrene, k_H, were measured in 0·1N- and 0·2N-perchloric acid by following the light absorption of the solutions at 2450 Å and at 2300 Å. In these measurements, the ampoules were filled with the reaction mixture nearly to the top in order to minimize the volume of the vapour phase. Initial rates were measured in solutions of styrene, of alcohol, and of styrene–alcohol mixtures of various compositions. The last yielded an estimate of the equilibrium composition which was consistent with the rate constants obtained from solutions containing only styrene or only alcohol.

[12] See, for example, Melander, *Arkiv Kemi*, 1954, **7**, 287.

Second-order rate constants (in sec.$^{-1}$ mole^{-1}) are as follows: k_{ol} at 30·4°, 1·2 × 10^{-7}; at 54·3°, 5 × 10^{-6}: k_H at 30·4°, 2 × 10^{-6}; at 54·3°, 1·4 × 10^{-5}. Owing to the slowness of these reactions, and because of the low solubility of styrene and its many side-reactions,[11] these rate constants are only semi-quantitative. Conservative estimates of the accuracy are ±50% for k_{ol}, and within a factor of two for k_H. Since these rate-constants are needed only to make small corrections to k_{rac} and k_{exch}, their accuracy is adequate.

Results

Racemization.—Experimental values of k_{rac} in aqueous perchloric acid are summarized in Table 2. It is seen that k_{rac} is independent of the alcohol concentration; reaction paths involving alcohol–alcohol interactions may therefore be neglected. On the other hand, there is a prounounced increase in k_{rac} with increasing perchloric acid concentration, which will be shown to be a neutral-salt effect. The rate constants in isotopically enriched water containing 2·2 atoms % of ^{18}O and 1·35 atoms % of D are on the average 3% greater than rate constants obtained under parallel conditions in ordinary water. Although this effect is not statistically significant, it is nevertheless in the right direction for an S_N1 mechanism in which a rapid, reversible proton addition to the alcohol is followed by a slow, unimolecular decomposition of the conjugate acid.[13]

In 0·1M-perchloric acid, rate constants were obtained at several temperatures. Within experimental error, plots of log (k_{rac}/T) against ($1/T$) were linear, as shown by the agreement of the results in columns 5 and 6 of Table 2. The standard enthalpy and entropy of activation,

Table 2. *Second-order rate constants for the acid-catalysed racemization of 1-phenylethyl alcohol in aqueous perchloric acid.*

Temp.	$HClO_4$ (M) [a]	Alcohol (M) [a]	10^5k_{rac} [b] (sec.$^{-1}$ mole^{-1} l.)	10^5k_{rac} [c] (calc.)
	(1) Effect of alcohol concentration.			
30·40°	0·1033	0·022	1·48 [d]	—
		0·046	1·45	
		0·066	1·45	
	(2) Effect of acid concentration.			
30·40	0·0172	0·084	1·26 [e]	—
	0·0201	0·079	1·25	
	0·0826	0·078	1·34 [e]	
	0·1033	0·066	1·45	
	0·522	0·06	2·4 [d]	
	1·00	0·023	4·7 [d]	
54·30	0·0170	0·082	41·9 [e]	
	0·0199	0·073	39·7 [d]	
	0·1013	0·039	44·5	
	(3) Effect of temperature.			
30·40	0·1033	0·02—0·07	1·46 [d]	1·49
45·12	0·1027	0·04	13·6 [d]	13·0
54·27	0·1013	0·04	44·5	45·5
64·36	0·1018	0·04	167	167

[a] Corrected for solvent expansion. [b] Eqn. 2. [c] $\log k/T = 12{\cdot}624 - 6051{\cdot}34/T$. [d] Average value, obtained in two or more runs. [e] In isotopically enriched water, containing 2·2 atoms % of ^{18}O and 1·35 atoms % of D.

computed from the data *via* the transition-state theory, were as follows: $\Delta H^{\ddagger}$, 27·68 kcal.; $\Delta S^{\ddagger}$, 10·55 e.u.

It was thought just possible that part of the increase in k_{rac} with increasing perchloric acid concentration is due to a bimolecular displacement reaction involving perchlorate ion and ROH_2^+, followed by rapid solvolysis of the perchlorate ester. To test this hypothesis, k_{rac} was measured also in aqueous hydrochloric and hydrobromic acid, with the results shown in Table 3. If there were appreciable S_N2 reaction with anions, displacement by bromide ion would be 4—60 times as fast as displacement by chloride ion,[14] and k_{rac} in hydrobromic acid would be

[13] Wiberg, *Chem. Rev.*, 1955, **55**, 713.
[14] See, *e.g.*, de la Mare, Fowden, Hughes, Ingold, and Mackie, *J.*, 1955, 3234.

considerably faster than in hydrochloric acid. Actually, no significant difference in rate is observed. The effect is therefore genuinely a neutral-salt effect.

TABLE 3. *Second-order rate constants* ($10^5 k_{rac}$, *sec.*$^{-1}$ *mole*$^{-1}$ *l.*) *for the acid-catalysed racemization of* 1-*phenylethyl alcohol in aqueous acids at* 30·4°.

Acid concn. (M)	HCl [a]	HBr [a]	$HClO_4$
0·02	1·4	1·5	1·25
0·10	1·8	1·7	1·46
0·47	2·0	2·3	2·3

[a] These rate constants are accurate only to 15% since the alcohol used in the rate determinations was unfortunately of low optical purity.

Oxygen Exchange.—The rate constants for oxygen exchange are listed in Table 4, together with values of k_{rac} measured under identical conditions. The latter have been corrected for the amount of racemization due to olefin formation to give the rate constants, $k'_{rac} = k_{rac} - k_{ol}$, resulting specifically from the substitution reaction. Comparison of k_{exch} with k'_{rac} provides an index of reaction mechanism. Within their standard error of 0·04, the three measured ratios of k_{exch}/k'_{rac} are equal, the mean value being 0·82. If the mechanism were S_N2, this ratio would be 0·5; if it were S_N1 and proceeded through an unshielded carbonium ion, the ratio would be 1·00. The intermediate magnitude of the observed ratio indicates either that there is some shielding of the front side of the carbonium ion by the departing OH_2 molecule, or that substitution proceeds simultaneously by both mechanisms. A quantitative interpretation will be given in the next section.

TABLE 4. *Summary of oxygen-exchange and related results.*

Temp.	$HClO_4$ (M)	$10^5 k_{exch}$ [a]	$10^5 k_{rac}$	$10^5 k'_{rac}$ [b]	k_{exch}/k'_{rac}
30·40°	0·0172	1·05	1·26	1·25	0·84
30·40	0·0826	1·09	1·34	1·33	0·82
54·31	0·0170	33·0	41·9	41·4	0·80

[a] Eqn. 1. [b] $k'_{rac} = k_{rac} - k_{ol}$.

DISCUSSION

Simplified Model for Shielding by the Departing Group.—It seems safe to assume that the solvolysis of 1-phenylethyl compounds in water and other good ionizing solvents proceeds by an S_N1 mechanism, and that the observed deviation of k_{exch}/k'_{rac} is due to shielding by the departing group. In support of this assumption, the solvolysis of optically active 1-phenylethyl chloride leads to virtually the same steric result (83% racemization, 17% inversion of configuration) in water [15] as it does in glacial acetic acid,[16] a solvent of much lower nucleophilic power. To give a rigorous description of the mechanism of shielding is complicated because the mechanism of solvolysis is so complicated. Winstein and his co-workers [17] write equation (3) for the ionization–dissociation process of RX and show that this mechanism, even though involving two

$$RX \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{\text{Intimate ion-pair}}{R^+X^-} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \underset{\text{Solvent-separated ion pair}}{R^+||X^-} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} R^+ + X^- \qquad \ldots \quad (3)$$

discrete ion-pair intermediates, is yet the simplest that will fit their large body of results.[17,18] Substitution may occur at R^+X^-, at $R^+||X^-$, or at R^+, and it is only after the system has

[15] Hughes, Ingold, and Scott, *J.*, 1937, 1201.
[16] Steigmann and Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 2536.
[17] Winstein, Clippinger, Fainberg, Heck, and Robinson, *J. Amer. Chem. Soc.*, 1956, **78**, 328.
[18] Fainberg and Winstein, *J. Amer. Chem. Soc.*, 1956, **78**, 2763, 2767, 2780; Fainberg, Robinson, and Winstein, *ibid.*, 1956, **78**, 2777; Winstein and Clippinger, *ibid.*, 1956, **78**, 2784.

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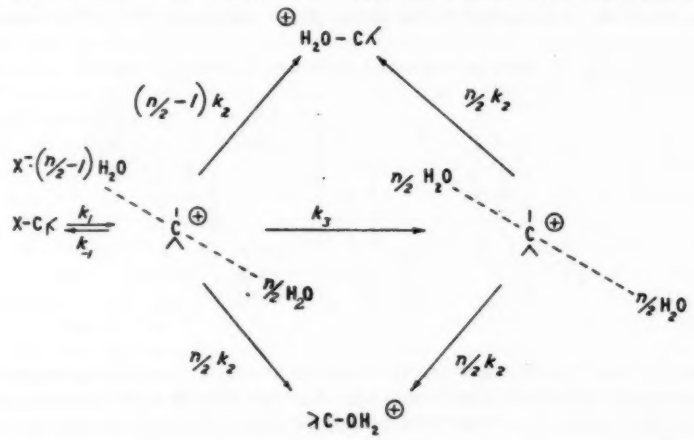
reached this last stage that the subsequent product is completely racemic. To predict the steric result for any given RX and solvent requires knowledge of as many as five reactivity ratios.

To render the problem manageable, we consider the *special* case where the carbonium ion is quite unstable. R^+X^- then reacts with solvent at a specific rate comparable with, or greater than, k_2. Further, since reaction with solvent proceeds with very low activation energy, the transition state will resemble R^+,[19] and the rate will be rather insensitive to changes in nucleophilic and electrophilic activity [19, 20] such as are caused by the proximity of the departing group X^-. On this basis a simplified kinetic scheme was obtained which is illustrated for hydrolysis in Fig. 1. Shielding by X^- is effective only in the intimate ion pair which reacts with solvent with rate constant $(n-1)k_2$, where k_2 is the " rate

FIG. 1. *Kinetic scheme showing the shielding of a carbonium ion by the departing group.*



constant " for a single solvent molecule when occupying the same site as X^-. The rate constant for reaction of solvent with $R^+||X^-$ and R^+ is written as nk_2, which assumes not only that k_2 is insensitive to the presence of X^-, but also that in the absence of X^- the arrangement of the water molecules immediately adjacent to R^+ resembles that when X– is a nearest neighbour, the X^- taking the place of one of the water molecules. The structure of X must therefore be such that the area of contact between X^- and the carbonium ion is roughly equal to that between a water molecule and the carbonium ion. Since the carbonium ion is quite reactive, k_{-3} is neglected compared with nk_2. According to this mode, the fractional excess of product with inverted configuration—that is, [inverted product — retained product]/[total product]—is equal to

$$f = 1/(n - 1 + k_3/k_2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The model will likewise accommodate the rates of acid-catalysed racemization and oxygen exchange of alcohols. With reference to Fig. 1, $X = OH_2$, hence $k_{-1} = k_2$. If olefin formation is discounted, $k'_{rac} = k_1$, and hence

$$k_{exch}/k'_{rac} = (n - 1 + k_3/k_2)/(n + k_3/k_2) \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Except for neglect of k_{-3} and small kinetic isotope effects on k_2, eqn. (5) is exact.

Subject to the simplifying assumptions which have been made, equations (4) and (5) serve as a single basis for interpreting (*a*) steric results for different groups X in the same

[19] Leffler, *Science*, 1953, **117**, 3039.
[20] Streitwieser, *Chem. Rev.*, 1956, **56**, 627.

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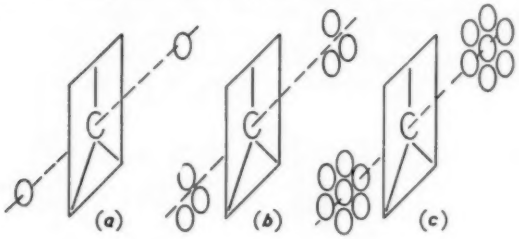
solvent, and (*b*) steric results for any one group X in different solvents. Of the parameters involved, k_2 is a function of the solvent, and k_3 is a function of both the solvent and X. A purely formal definition of n has already been given but it is instructive to examine this quantity in greater detail. Referring to Fig. 2, we recognize three somewhat idealized models for the manner in which the carbonium ion may react with molecules in its solvation shell. Fig. 2(*a*) shows reaction as taking place only from the two nearest-neighbour sites just above and just below the central C^+-atom; hence $n = 2$. Fig. 2(*b*) shows another possible model in which the nearest-neighbour sites are arranged symmetrically about the normal to the plane of the carbonium ion passing through C^+. In the example shown, $n = 6$. Fig. 2(*c*) differs from 2(*a*) in that reaction can occur also from next-nearest-neighbour sites, though in general with lower probability. Since X in R^+X^- occupies a nearest-neighbour site, the effective value of n is in the range 2—14. Model 2(*c*) implies that covalent-bond formation to C^+ can occur efficiently even from directions which are not normal to the plane of the carbonium ion. The model is made

FIG. 2. *Some possible models of the solvated carbonium ion.*



credible by the fact that in displacement reactions involving a neighbouring group [21] or an S_Ni mechanism the attacking direction is also at a considerable angle from the normal, and even in S_N2 displacement a model with flexible directions of attack is more successful than a rigid one.[22]

Regardless of model, the total range of plausible values for n is seen to be small. For any one carbonium ion the range is likely to be even smaller and, if the solvents in which steric results are obtained are of similar type (*e.g.*, hydroxylic) and molar volume, n may well be quite constant.

Results for the 1-*Phenylethyl System.*—For $Ph{\cdot}CH(OH_2^+){\cdot}CH_3$ in water, $k_{exch.}/k'_{rac} = 0{\cdot}82 \pm 0{\cdot}04$, hence from eqn. (5), $n + k_3/k_2 = 6 \pm 1$. For $Ph{\cdot}CHCl{\cdot}CH_3$ in water, $f = 0{\cdot}17 \pm 0{\cdot}02$,[15] hence from eqn. (4), $n + k_3/k_2 = 6{\cdot}9 \pm 0{\cdot}8$. Within experimental error, the two values are equal. Steric results for the S_N1 solvolysis of 1-phenylethyl chloride are also available in other one-component solvents.[15,16] After correction for the S_N2 process, values of f are 0·22 in methanol at 70°, 0·28 in ethanol at 70°, and 0·16 in glacial acetic acid at 50°. The corresponding values of $n + k_3/k_2$ are, respectively, 5·4, 4·6, and 7·3. For 1-phenylethyl toluene-*p*-sulphonate, steric results very similar to those for the chloride have been reported in ethanol and glacial acetic acid,[23] although these results are still to be corrected for the S_N2 process and racemization of the solvolysis products.

The striking feature of the values of $n + k_3/k_2$ is their apparent insensitivity to changes in the nature, particularly charge type, of the departing group, and of the solvent over such wide ranges of solvent properties. The minimum value $n = 2$ being taken, the entire variation of k_3/k_2 is within a factor of 2, and for the two values in water the maximum variation is even smaller. On electrostatic grounds one would have expected the value of

[21] Winstein, Grunwald, and Ingraham, *J. Amer. Chem. Soc.*, 1948, **70**, 821.
[22] de la Mare, Fowden, Hughes, Ingold, and Mackie, *J.*, 1955, 3200.
[23] Kenyon, Phillips, and Taylor, *J.*, 1933, 173.

k_3/k_2 in water to be appreciably greater for OH_2 than for Cl^-, although admittedly this effect may be compensated by solvation effects.

The simplest and, to us, most attractive theory which will account for the results is that k_3/k_2, though not necessarily constant, *is small compared with* n, at least in water, methanol, and ethanol. This means that substitution occurs mainly at the intimate ion-pair stage but, since $n \approx 6$, from more than two sites. The small decrease in n on changing from water to methanol and ethanol can result from the larger size of the alcohol molecules. On this basis, the somewhat larger value obtained in acetic acid indicates that k_3/k_2 is now not negligible.

Steric results for the solvolysis of 1-phenylethyl chloride are available also in acetone–water mixtures.[15] Here the product is more nearly racemic, f being 0·05 in 60% acetone and 0·02 in 80% acetone. However, since this is a two-component solvent, the result may be due to preferential solvation rather than a large value of k_3/k_2. The presence of the departing chloride ion may cause strong preferential solvation of the "front" of the carbonium ion by water, which can form hydrogen bonds to chloride, whereas no such inducement for solvation by water exists at the "back." We may therefore expect to find more acetone molecules at the back than at the front, and this partially counterbalances the shielding by chloride at the front.

Results for sec.-*Butyl and* 1-*Methylheptyl System.*—The solvolysis of optically active 1-methylheptyl bromide in 60% ethanol proceeds with $f \approx 0{\cdot}70$.[24] * If k_3/k_2 is assumed to be small, $n = 2{\cdot}4$ from eqn. (4). Hence, for the acid-catalysed racemization and oxygen exchange of the alcohol, it can be predicted from eqn. (5) that $k_{exch.}/k_{rac} = 0{\cdot}58$. The actual value of k_{exch}/k_{rac} for 1-methylheptyl alcohol is not available, but Bunton, Konasiewicz, and Llewellyn[3] have reported a value of 0·5 for this ratio for the mechanistically similar *sec.*-butyl alcohol. Although this is a typical result for an S_N2 process, they describe the mechanism as S_N1. Our examination of their data supports this view, and we find that the most probable value is actually 0·52, and even this value may be somewhat too small owing to medium effects: the alcohol concentration in the exchange experiments averaged 1·3M, but was only about 0·8M in the racemization experiments. Although the published data suffice to show that the medium effect due to this discrepancy is not large, an effect of the order of 10—20% is quite possible and, judged by the data for *tert.*-butyl alcohol,[2] its direction would be such as to make k decrease with increasing alcohol concentration.

Although it appears probable that both the 1-phenylethyl and the *sec.*-butyl or 1-methylheptyl compounds solvolyse by mechanism S_N1 in the sense that a metastable intermediate is involved, there are some important differences. From the effect of changing the nucleophilic power of the solvent on the solvolysis rate one can conclude that there is some "push" by solvent in the formation of the intermediate in the secondary alkyl system, but that this is negligible in the 1-phenylethyl system.[25,26] The present work suggests two additional aspects in which S_N1 reactions may differ: the effective number, n, of sites from which substitution can occur, and the relative magnitudes of the rates of substitution and of dissociation of the intimate ion-pair intermediate. For the more reactive intermediates, products may be formed largely at the intimate ion-pair stage even though specific nucleophilic driving force was not required in the prior ionisation step.

Salt Effect on k_{rac} *and the* H_0-*Function.*—In acid-catalysed reactions in which a rapid, reversible, simple proton addition to a substrate is followed by a slow reaction of the conjugate acid, the method of Zucker and Hammett[27] has often been applied to reactions

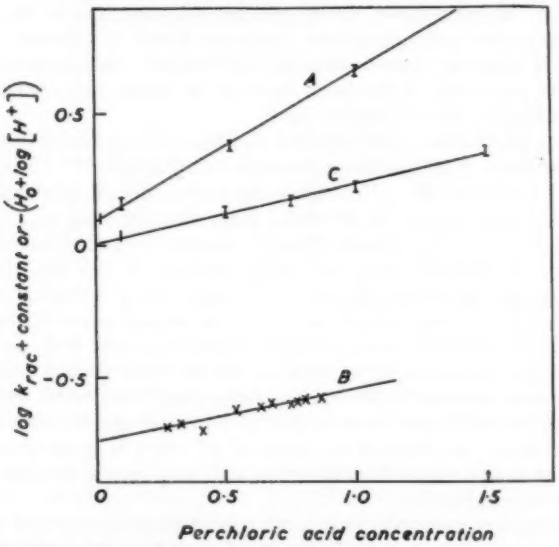
* Preferential solvation does not appreciably affect the average steric result when both solvent components are hydroxylic.

[24] Hughes, Ingold, and Masterman, *J.*, 1937, 1196.
[25] Winstein, Grunwald, and Jones, *J. Amer. Chem. Soc.*, 1951, **73**, 2700.
[26] Coburn, Grunwald, and Marshall, *ibid.*, 1953, **75**, 5735.
[27] Zucker and Hammett, *ibid.*, 1939, **61**, 2791.

in aqueous media to determine whether there is participation by a water molecule in the slow reaction step.[3, 27, 28-31] According to this method, if there is no participation, the pseudo-first order rate constant of the substrate is proportional to antilog $(-H_0)$, where H_0 is the acidity function;[32] if there is participation, the rate is proportional to the acid concentration.

The application of this method to our results is shown in Fig. 3. In following the conventional representation of salt effects,[33] $\log k_{rac}$ is plotted against perchloric acid concentration. The slope of the resulting straight line, 0·574, is much greater than the slope, 0·232, of the nearly linear plot of $-(H_0 + \log [H^+])$, where $[H^+]$ is the acid concentration. Evidently the rate is not proportional to antilog $(-H_0)$. A possible explanation of the large slope is that the transition state from $Ph{\cdot}CH(OH_2^+){\cdot}CH_3$ resembles a

FIG. 3. *Salt effects in aqueous perchloric acid.*



A; 1-Phenylethyl alcohol at 30·4°, slope 0·574 (from Table 2).
B; *sec.*-Butyl alcohol (the data reported at acid concentrations less than 0·25M show considerable scatter and are not shown) (from Bunton, Konasiewicz, and Llewellyn, *J.*, 1955, 604).
C; $-(H_0 + \log [H^+])$. Values of H_0 from Paul and Long, *Chem. Rev.*, in the press.

carbonium ion. The slope of $\log k_{rac}$ against $[H^+]$ would then resemble that of $-(C_0 + \log [H^+])$, where C_0 is the acidity function applicable to equilibria leading to carbonium ions.[34] Recent unpublished results by Professor Deno indicate that the average value of this slope is about 1·0 in the range 0—1M-perchloric acid. The observed magnitude of the salt effect on $\log k_{rac}$ is therefore intermediate between that expected from the two acidity functions, but is not represented accurately by either.

Also shown in Fig. 3 are the data for the acid-catalysed racemization of *sec.*-butyl alcohol.[3] The slope, −0·198, is very nearly equal to that for $-(H_0 + \log [H^+])$, indicating

[28] Long, Dunkle, and McDevit, *J. Phys. Chem.*, 1951, **55**, 829.
[29] Paul, *J. Amer. Chem. Soc.*, 1952, **74**, 141.
[30] Taft, *ibid.*, 1952, **74**, 5372.
[31] Pritchard and Long, *ibid.*, 1956, **78**, 2667.
[32] Hammett and Deyrup, *ibid.*, 1932, **54**, 4239. For a recent review see Paul and Long, *Chem. Rev.*, in the press.
[33] Ciapetta and Kilpatrick, *J. Amer. Chem. Soc.*, 1948, **70**, 639.
[34] Deno, Jaruzelski, and Schriesheim, *ibid.*, 1955, **77**, 3044.

that water does not participate in the rate-determining ionization. This finding conflicts with evidence from solvent effects which indicates that there is participation by solvent in the mechanistically similar solvolysis of *sec.*-butyl bromide.[26] While further work is needed to clear up this discrepancy, the striking difference between the salt-effects for 1-phenylethyl alcohol and *sec.*-butyl alcohol, the recent indications that there may be structural limitations to the correlation of acid–base equilibria by H_0,[35] and previous examples of acid-catalysed reactions whose rates are not correlated neatly by one or the other of the acidity functions [36-38] cause us to feel that the theory of Zucker and Hammett, in the simple form in which it was originally suggested,[27] may not provide a consistently reliable basis for the diagnosis of reaction mechanism.

We thank Dr. I. Dostrovsky and Dr. D. Samuel for helpful discussions, and Dr. N. C. Deno for data on the C_0 function before publication. One of us (E. G.) thanks the Yad Chaim Weizmann for a Weizmann Memorial Fellowship.

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[35] N. C. Deno, lecture presented before the Sixth Conference on Reaction Mechanisms, Swarthmore, Penna., September, 1956; Deno and Perizzolo, *J. Amer. Chem. Soc.*, 1957, **79**, 1345.
[36] Bell, Dowding, and Noble, *J.*, 1955, 3106.
[37] Gold and Hilton, *J.*, 1955, 843.
[38] Long and McIntyre, *J. Amer. Chem. Soc.*, 1954, **76**, 3240, 3243.

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508. *Spectroscopic Studies. Part I. 2:4-Dinitrophenylhydrazones in Neutral and in Alkaline Solutions.**

By C. J. TIMMONS.

The absorption spectra of numerous 2:4-dinitrophenylhydrazones have been studied in various neutral and alkaline solutions, and the results for all the bands have been classified. The charge-transfer spectra of the ions are complementary to the charge-resonance spectra of the neutral molecules in correlating spectra with the structures of the parent carbonyl compounds. Solvent shifts, including those due to hydrogen bonding and π-complex interaction, are discussed. Further cases are reported of the formation of 2:4-dinitrophenylhydrazones in pyridine solution.

2:4-DINITROPHENYLHYDRAZONES have been employed extensively for characterisation of carbonyl compounds, particularly in the last thirty years,[1,2] Their utility has been considerably enhanced by detailed knowledge of the correlation between their light-absorption properties and the structures of the parent carbonyl compounds.[3-10] Although it has been known that 2:4-dinitrophenylhydrazones give red to blue colours with

* Presented in part at the European Molecular Spectroscopy Group Conference, Oxford, July, 1955.

[1] (*a*) Curtius and Dedichen, *J. prakt. Chem.*, 1894, **50**, 241; Purgotti, *Gazzetta*, 1894, **24**, 554; (*b*) Brady and Elsmie, *Analyst*, 1926, **51**, 77; Brady, *J.*, 1931, 757.
[2] Allen, *J. Amer. Chem. Soc.*, 1930, **52**, 2955.
[3] Braude and Jones, *J.*, 1945, 498.
[4] Roberts and Green, *J. Amer. Chem. Soc.*, 1946, **68**, 214.
[5] Ramirez and Kirby, *ibid.*, 1952, **74**, 4331; 1953, **75**, 6026; 1954, **76**, 1037.
[6] Bohlmann, *Chem. Ber.*, 1951, **84**, 490.
[7] Fleisher and Kendall, *J. Org. Chem.*, 1951, **16**, 556.
[8] Djerassi and Ryan, *J. Amer. Chem. Soc.*, 1949, **71**, 1000; Johnson, *ibid.*, 1953, **75**, 2720; Reich, Crane, and Sanfilippo, *J. Org. Chem.*, 1953, **18**, 822; Reich and Samuels, *ibid.*, 1954, **19**, 1040; Barany and Pianka, *J.*, 1953, 2217; Heilmann, Gaudemaris, and Arnaut, *Compt. rend.*, 1952, **234**, 1177; Heilmann, Gaudemaris, and Noack, *Bull. Soc. chim. France*, 1954, 990, 992; Pestemer and Brück in "Methoden der Organischen Chemie (Houben-Weyl)," 4th edn., Ed. Müller, 1955, Vol. III, Part 2, p. 675.
[9] Braude, Jones, Koch, Richardson, Sondheimer, and Toogood, *J.*, 1949, 1890.
[10] Braude and Timmons, *J.*, 1953, 3144.

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Table 1. *Absorption bands of representative 2 : 4-dinitrophenylhydrazones and related compounds in neutral and alkaline (N/100) ethanol.*†

The first figure in each column is the wavelength of the maximum in mμ and the second figure the extinction coefficient ($10^{-3}\varepsilon$). Figures in italics denote submerged bands estimated graphically (see Experimental section).

		Neutral								Alkaline							
		E_0 band		E_1 band		E_2 band		B band		E_0^- band		E_1^- band		E_2^- band		NO_2^- band	
No.	Compound																
1	C_6H_6 [a]	150	—	184	46	203	7 [a]	255	0·2 [a]	—	—	—	—	—	—	—	—
2	$Ph{\cdot}NH_2$ [b]	—	—	198	20	235	7	280	1·3	—	—	—	—	—	—	—	—
3	$Ph{\cdot}NO_2$ [f]	200	20	213	15	259	7·5	*294*	*2·0*	—	—	—	—	—	—	—	—
4	$o\text{-}NO_2{\cdot}C_6H_4{\cdot}NH_2$ [c]	—	—	231	17	276	5	402	5·5	—	—	—	—	490	>3	—	—
5	$p\text{-}NO_2{\cdot}C_6H_4{\cdot}NH_2$	—	—	229	7	371	15·5	—	—	—	—	—	—	—	—	—	—
6	$p\text{-}NO_2{\cdot}C_6H_4{\cdot}NH{\cdot}N{:}CMe_2$ [c]	—	—	249	10·5	390	23	—	—	—	—	319	4·5	510	33·5 [a]	—	—
7	$m\text{-}(NO_2)_2C_6H_4$ [c,f]	—	—	234	18	—	—	285	0·9 [a]	—	—	—	—	—	—	536	15 [i]
8	$2:4\text{-}(NO_2)_2C_6H_3{\cdot}NH_2$ [c]	223	11·5	257	10·5	336	16	*388*	*7*	*280*	*6*	386	19·5	*412*	*4·5*	531	14
9	$2:4\text{-}(NO_2)_2C_6H_3{\cdot}NH{\cdot}NH_2$ [c,d]	219	12	258	9·5	350	14·5	*410*	*5·5*	—	—	—	—	526	17	*590*	*3·5* [a]
10	$2:4\text{-}(NO_2)_2C_6H_3{\cdot}NH{\cdot}NHAc$ [g]	209	12	256	10	332	14	*380*	*3*	*280*	*6*	—	—	424	18·5	*530*	*4·5*
	Dinitrophenylhydrazones of:																
11	Me·CHO (m. p. 168°)	—	—	—	—	357	21	*424*	*5*	—	—	—	—	424	18·5	506	9
12	Me_2CO	227	18·5	*265*	9·5	357	20·5	*430*	*5*	*260*	*10*	—	—	431	19·5	520	11·5
13	$n\text{-}C_5H_{11}{\cdot}C{\equiv}C{\cdot}CHO$ [c,d]	—	—	—	—	357	23·5	*415*	*4*	—	—	345	6	498	27·5	*575*	*6·5*
14	$Me_2C{:}CH{\cdot}COMe$	248	14	*279*	*9*	379	24	*450*	*7*	—	—	*360*	*6·5*	451	20·5	*555*	*11·5*
15	$Me_2C{:}CH{\cdot}CO{\cdot}CH{:}CMe_2$ [c]	*257*	*16*	*291*	*7·5*	385	29	*459*	*6*	—	—	360	4	492	28·5	*586*	*13·5*
16	$Me_2C{:}CH{\cdot}CH{:}CH{\cdot}COMe$	268	17	303	18·5	390	35	*463*	*8·5*	284	22	*360*	*6·5*	479	31	*575*	*13·5*
17	$CH_2{:}CH{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}COMe$	—	—	314	20·5	398	38·5	*475*	*10*	300	20·5	—	—	497	35·5	*605*	*10*
18	Retinene$_1$	—	—	*354*	*23*	437	59·5	*507*	*14·5*	*330*	*14·5*	371	26	518	62·5	—	—
19	Ph·COMe	*262*	*12·5*	*288*	*8*	373	27·5	*434*	*7*	—	—	*356*	*6*	462	24·5	*550*	*15*
20	Ph·CH:CH·COMe	*271*	*13*	303	15·5	391	35	*465*	*8*	—	—	—	—	488	34	*583*	*12·5*
21	2-Cinnamylidene*cyclo*hexanone	—	—	327	22·5	408	30·5	*480*	*11*	319	20	—	—	488	30	592	11·5
22	Et·CO·COPr (mono)	—	—	—	—	351	23·5	*404*	*7·6*	—	—	—	—	512	34	—	—
23	Et·CO·COPr (bis)	—	—	—	—	392	38	*451*	*28*	—	—	354	11	558	44·5	—	—

[a] Unstable.

† In some cases 10% $CHCl_3$–EtOH (v/v) was used which obscured shorter-wavelength bands.

[a] In heptane; Platt and Klevens, *Chem. Rev.*, 1947, **41**, 301. [b] In MeOH; Ley and Specker, *Ber.*, 1939, **72**, 192. [c] Alkaline spectra in $H{\cdot}CO{\cdot}NMe_2$. [d] N/50-NaOH. [e] In hexane; fine structure also present. [f] Wenzel, *J. Chem. Phys.*, 1954, **22**, 1623. [g] Ref. 1*a*. [h] Table 2, ref. *i*. [i] 0·1N-NaOH.
References to other compounds are given in Table 2.

alkali,[1a,4,7,11,12] until recently no detailed spectroscopic studies of these colours had been reported. Since this work began two groups [13] have deduced correlations between the spectra in alkaline solution and the structure of the parent carbonyl compound for a limited range of carbonyl compounds. The results now described permit more detailed correlations for a wider range of saturated, variously unsaturated, and substituted carbonyl compounds, similar in general to the correlations in neutral solution. There are however some important differences between the two series, which give additional information about the carbonyl compound.

The spectra in various neutral solvents have also been studied and these permit an explanation of the varied solvent and substituent effects previously noted [3,5,7,10] for the main absorption band, as well as allowing the other bands to be classified.

Neutral Solvents.—In general 2 : 4-dinitrophenylhydrazones show four absorption bands, two at shorter wavelengths than the main maximum and one at longer wavelengths, but these are not always all resolved as discrete bands, owing to considerable overlap. In most cases, it is possible to estimate the majority of the submerged bands graphically and these are included in Table 1 in italics. Each of these bands shifts to longer wavelengths as the number of conjugated double bonds in the carbonyl compound increases, as has been shown previously for the main band.[3] The dependence of the wavelengths of the maxima of all four bands on the number of double bonds (n) in aliphatic or mainly aliphatic compounds is illustrated in Fig. 1, where the squares of the wavelengths are plotted against the number of double bonds. The behaviour of the three subsidiary bands (E_0, E_1, B) parallels that of the main band (E_2) in conforming reasonably well to a linear relation $\lambda^2 \propto n$. The range of n studied is too small for a rigorous test of this relation and in fact the simpler relation $\lambda \propto n$ fits only slightly less accurately (particularly over the range $0 \leqslant n \leqslant 3$). By analogy with other polyene systems the λ^2 relation would be expected.

Comparison of the four bands in the 2 : 4-dinitrophenylhydrazones with those for related aromatic compounds and for benzene itself as indicated in Table 1, suggests that they may be displaced benzene absorption bands, as argued by Doub and Vandenbelt [14] for other substituted aromatic systems. For this reason, the three long-wavelength bands in the 2 : 4-dinitrophenylhydrazones have been designated E_1, E_2, and B bands [15] and the short-wavelength band, which may correspond to a band at 150 mμ in benzene, is now called the E_0 band. In the 2 : 4-dinitrophenylhydrazones, the intensity of the E_0 band shows only small variations, in contrast to the intensities of the E_1, E_2, and B bands, which increase regularly with n.

For diagnostic purposes the E_2 band is the most useful, and for this reason the other bands have received scant attention in the past. In general, bands below 270 mμ are of little use as most dinitrophenylhydrazones are difficultly soluble in solvents transparent below 270 mμ. However, the position of the E_1 band distinguishes fully conjugated from cross-conjugated dienone derivatives. Cinnamylidene*cyclo*hexanones are unusual in having a particularly intense E_1 band (nos. 21 and 83).

[11] Strain, *J. Amer. Chem. Soc.*, 1935, **57**, 758.

[12] Lappin and Clark, *Analyt. Chem.*, 1951, **23**, 541; Gornall and Macdonald, *J. Biol. Chem.*, 1953, **201**, 279; Hadley, Hall, Heap, and Jacobs, *J.*, 1954, 1421; Isherwood and Cruickshank, *Nature*, 1954, **173**, 121; Isherwood and Jones, *ibid.*, 1955, **175**, 419; Barrenscheen and Dreguss, *Biochem. Z.*, 1931, **233**, 305; Neuberg and Kobel, *ibid.*, 1928, **203**, 463; Raistrick and Rudman, *Biochem. J.*, 1956, **63**, 395; Schepartz and Daubert, *J. Amer. Oil Chemists' Soc.*, 1950, **27**, 267; Cavallini and Frontali, *Ricerca sci.*, 1953, **23**, 807; Pesez and Poirier, "Méthodes et Réactions de l'Analyse organique," Masson, Paris, 1954, Vol. III, p. 124; Pucher, Vickery, and Wakeman, *Ind. Eng. Chem. Anal.*, 1934, **6**, 288; Wolf, *Z. analyt. Chem.*, 1952, **136**, 401; Daniels, Scholes, and Weiss, *J.*, 1956, 832; Mendelowitz and Riley, *Analyst*, 1953, **78**, 704; Banks, Vaughn, and Marshall, *Analyt. Chem.*, 1955, **27**, 1348.

[13] Yamaguchi, Fukushima, Tabata, and Ito, *J. Pharm. Soc. Japan*, 1954, **74**, 1335; Jones, Holmes, and Seligman, *Analyt. Chem.*, 1956, **28**, 191.

[14] Doub and Vandenbelt, *J. Amer. Chem. Soc.*, 1947, **69**, 2714; 1949, **71**, 2414; 1955, **77**, 4535.

[15] Braude and Nachod, "Determination of Organic Structures by Physical Methods," Academic Press, New York, 1955, p. 150.

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Considering now only the E_2 band, the majority of 2 : 4-dinitrophenylhydrazones show a hypsochromic shift in hydroxylic solvents compared with chloroform solutions (see Table 2 and Fig. 2). The minority that show bathochromic shifts are derivatives of aldehydes and of carbonyl compounds with α-hydroxy(but not alkoxy)-substituents, and the related compounds 2 : 4-dinitroaniline (no. 8), 2 : 4-dinitrophenylhydrazine (no. 9), 2 : 4-dinitrophenylacethydrazide (no. 10), and acetone *p*-nitrophenylhydrazone

FIG. 1. *Plot of squares of the wavelengths of various absorption bands of 2 : 4-dinitrophenylhydrazones of polyene carbonyl compounds against the number of double bonds in the parent carbonyl compounds.*

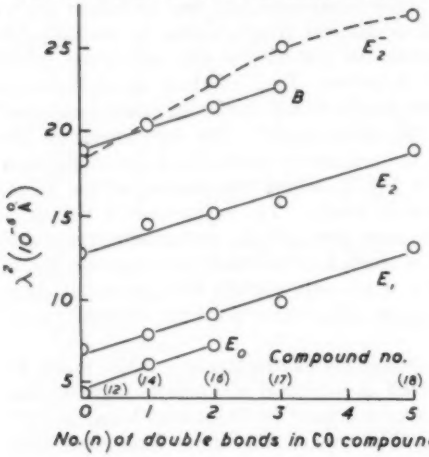
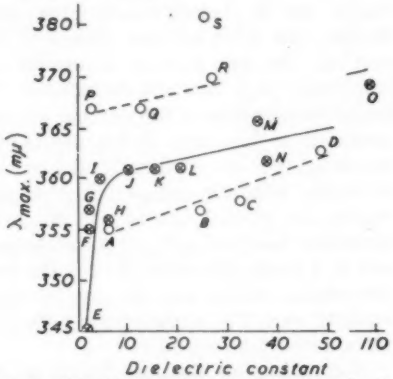


FIG. 2. *Plot of wavelength of main band of acetone 2 : 4-dinitrophenylhydrazone in various solvents against dielectric constant of solvent* (cf. *Weissberger, Proskauer, Riddick, and Toops, "Technique of Organic Chemistry," 1955, Vol. VII, Interscience Pub. Inc., New York*).



A, Acetic acid; *B*, ethanol; *C*, methanol; *D*, 80% v/v aqueous methanol; *E*, cyclohexane; *F*, dioxan; *G*, benzene; *H*, ethyl acetate; *I*, chloroform; *J*, methylene dichloride; *K*, pentan-2-one; *L*, acetone; *M*, nitromethane; *N*, acetonitrile; *O*, formamide; *P*, carbon disulphide; *Q*, pyridine; *R*, dimethylformamide; *S*, benzonitrile.

(no. 6) (λ in $CHCl_3$ − λ in EtOH = −4, −7, −6, and −7 respectively). A study of solvent shifts with a typical example of the major group, acetone dinitrophenylhydrazone, summarised in Fig. 2 for a wider range of solvents, shows that the solvents fall into three

TABLE 2. *Main maxima* (mμ) *and* pK_a' *of dinitrophenylhydrazones of various carbonyl compounds.*

* Unstable. † In $CHCl_3$

(*a*) Bryant, *J. Amer. Chem. Soc.*, 1938, **60**, 2814; (*b*) Woods and Sanders, *ibid.*, 1946, **68**, 2111; (*c*) Braude and Timmons, *J.*, 1953, 3131; (*d*) Brown, Armstrong, Moyer, Anslow, Baker, Querry, Bernstein, and Safir, *J. Org. Chem.*, 1947, **12**, 160; (*e*) Lauchenauer and Schinz, *Helv. Chim. Acta*, 1949, **32**, 1265; (*f*) Owen, personal communication; cf. Experimental section; (*g*) Campbell, *Analyst*, 1936, **61**, 391; (*h*) Sobotka and Chanley, *J. Amer. Chem. Soc.*, 1949, **71**, 4136; (*i*) Ansell, Hickinbottom, and Hyatt, *J.*, 1955, 1592; (*j*) Braude and Timmons, *J.*, 1953, 3313; (*k*) Braude and Evans, *J.*, 1955, 3334; (*l*) Naves and Ardizio, *Bull. Soc. chim. France*, 1954, 330; (*m*) Crombie, *J.*, 1955, 1007; (*n*) Blum and Gaudemaris, *Bull. Soc. chim. France*, 1954, 996; (*o*) Braude and Coles, *J.*, 1952, 1425; (*p*) Henbest, Shaw, and Woods, *J.*, 1952, 1154; (*q*) Vipond, personal communication; (*r*) Braude, Linstead, and Wooldridge, *J.*, 1956, 3070; (*s*) Braude, Jones, Sondheimer, and Toogood, *J.*, 1949, 607; (*t*) Ritchie, King, and Timmons, unpublished work; (*u*) Ahmad and Weedon, *J.*, 1953, 3815; (*v*) Braude and Timmons, *J.*, 1950, 2007; (*w*) Braude and Wheeler, *J.*, 1955, 329: structure is in agreement with the spectra; (*x*) *idem*, *ibid.*, p. 320; (*y*) Cheeseman, Heilbron, Jones, Sondheimer, and Weedon, *J.*, 1949, 2031; (*z*) Farrar, Hamlet, Henbest, and Jones, *J.*, 1952, 2657; (*aa*) Braude and Coles, *J.*, 1950, 2012; (*bb*) Bredereck, *Ber.*, 1932, **65**, 1833; Bredereck and Fritzsche, *Ber.*, 1937, **70**, 802; (*cc*) Braude and Webb, unpublished work; (*dd*) Braude, unpublished work; (*ee*) Braude and Coles, *J.*, 1950, 2014; (*ff*) Braude and Timmons, *J.*, 1950, 2000; (*gg*) Coe, Gale, Linstead, and Timmons, *J.*, 1957, 123; (*hh*) Heilbron, Jones, Smith, and Weedon, *J.*, 1946, 54; (*ii*) Menotti, *Ind. Eng. Chem. Anal.*, 1942, **14**, 418; (*jj*) McElvain and McKay, *J. Amer. Chem. Soc.*, 1955, **77**, 5601; (*kk*) King and Wilson, personal communication.

TABLE 2. *Main maxima* (mμ) *and* pK_a' *of dinitrophenylhydrazones of various carbonyl compounds.*

No.	Carbonyl compound	Neutral solvent: 10% $CHCl_3$ in EtOH λ	Neutral solvent: 10% $CHCl_3$ in EtOH $10^{-3}\varepsilon$	Neutral solvent: λ ($CHCl_3$) − λ (EtOH)	Solvent 0·01N in NaOH: 10% $CHCl_3$ in EtOH λ	Solvent 0·01N in NaOH: 10% $CHCl_3$ in EtOH $10^{-3}\varepsilon$	H·CO·NMe_2 λ	H·CO·NMe_2 $10^{-3}\varepsilon$	$-pK_a'$	Ref. (see p. 2616)
24	CH_2O	348	19·5	−1	428	18 *	—	—	3·2	2
25	Me·CHO (m. p. 147°)	357	20	−1	426	17	—	—	—	2
11	Me·CHO (m. p. 168°)	357	21	−2	424	18	439	20·5	3·0	*a*
26	Pr^n·CHO	356	20·5	0	431	19·5	—	—	—	2
27	Bu^t·CHMe·CH_2·CHO	358	21	−1	434	21	—	—	—	
28	HO·$[CH_2]_4$·CHO	358	22·5	0	428	19 *	—	—	—	*b*
29	HO·CMe_2·CHO	354	24	−5	429	19	—	—	2·8	*c*
30	EtO_2C·$[CH_2]_4$·CHO (m. p. 73°)	357	23	2	431	21	—	—	—	*d*
31	EtO_2C·$[CH_2]_4$·CHO (m. p. 54°)	357	22	—	431	20	—	—	—	*d*
32	2 : 6 : 6-Trimethyl*cyclo*hex-2-ene-1-aldehyde	360	24·5	1	435	24·5	—	—	—	*e*
33	Pyran-2-aldehyde	356	23	5	436	18	—	—	—	*f*
12	Me_2CO	358	21	5	432	19	446	22	2·8	2
34	Bu^t·COEt	361	22·5	3	435	18	—	—	—	2
35	n-C_5H_{11}·COMe	361	22·5	5	435	21	—	—	—	2
36	Bu^t·COMe	359	23	5	432	19	—	—	—	2
37	2-Methyl*cyclo*pentanone	364	22	1	434	19	—	—	2·6	*g*
38	*cyclo*Hexanone	362	22·5	2	435	19	—	—	—	11
39	2 : 2 : 6-Trimethyl*cyclo*hexanone	360	22	5	432	16	—	—	2·8	*h*
40	HO·CMe_2·COMe (m. p. 71—72°)	357	21	−2	436	19·5	—	—	—	*c*
41	HO·CMe_2·COMe (m. p. 148°)	357	23	−2	437	22	—	—	—	*i*
42	CMe_2:CH·CMe(OH)·COMe	359	22·5	−3	436	22	—	—	—	*c*
43	Pr^n·CH(OH)·COEt	362	20	−1	436	20	—	—	—	10
44	Pr^i·CH(OH)·$COPr^i$ (m. p. 101°)	356	21	0	442	20·5	—	—	—	10
45	Pr^i·CH(OH)·$COPr^i$ (m. p. 147°)	371	27	3	438	25	—	—	—	10
46	EtO·CMe_2·COMe	357	23·5	4	439	19·5	—	—	—	
47	HO_2C·COMe	356	22	−5	442	17	—	—	—	2
48	HO_2C·$[CH_2]_3$·COMe	358	16·5	5	432	17	—	—	—	2
49	NC·CHMe·CH_2·COMe	355	21·5	−2	436	20·5	—	—	—	*j*
50	Me·CH:CH·CHO	374	27·5	—	456	29·5	464	30·5	—	3
51	*cyclo*Hex-1-enealdehyde	376	28·5	—	458	28·5	—	—	—	*k*
52	2 : 6 : 6-Trimethyl*cyclo*hex-1-enealdehyde	382	28·5	—	458	28·5	—	—	—	*l*
13	n-C_5H_{11}·C:C·CHO	357	22·5	—	451	6	498	27·5	—	*m*
53	CH_2:CMe·COMe	367	26	8	456	22·5	—	—	—	*n*
54	Me·CH:CH·COMe	375	25	8	453	24	476	27·5	—	*o*
14	Me_2C:CH·COMe	381	24		452	21	476	27	2·5	2
55	Bu^t·CH:CH·COMe	373	27·5	—	456	25	—	—	—	
56	1-Acetyl-4 : 4-dimethyl*cyclo*hexene	376	25	—	452	21·5	—	—	—	*p*
57	2-Ethylidene*cyclo*hexanone	378	23·5	5	445	21	476	26	—	*q*
58	Cholest-4-en-3-one	384	31	—	462	25·5	—	—	—	*r*
59	Me·CH:CH·CO·Bu^t	366	22·5	—	—	—	478	23	1·7	
60	Me_2C:CH·$COPr^i$	369	26·5	—	462	19·5	—	—	—	
61	1-Acetyl-2-methyl*cyclo*hexene	372	23·5	—	442	21	468	24	—	*s*
62	CH_2:C(OMe)·COMe (m. p. 173—175°)	366	19·5	—	454	22·5	—	—	—	
63	CH_2:C(OMe)·COMe (m. p. 147—149°)	363	23·5	3	490	24	—	—	3·3	
64	3-*iso*Propoxy*cyclo*hex-2-enone	395	26·5	3	456	24	—	—	—	
65	5-Chloro-3 : 3 : 6-trimethyl*cyclo*hexanone	374	28	—	468	26	—	—	—	*t*
66	Me·CH:CH·CH:CH·CHO	390	32·5	—	480	34·5	494	39	—	3

TABLE 2. (*Continued.*)

No.	Carbonyl compound	Neutral solvent: 10% $CHCl_3$ in EtOH λ	Neutral solvent: 10% $CHCl_3$ in EtOH $10^{-3}\varepsilon$	Neutral solvent: λ ($CHCl_3$) − λ (EtOH)	Solvent 0·01N in NaOH: 10% $CHCl_3$ in EtOH λ	Solvent 0·01N in NaOH: 10% $CHCl_3$ in EtOH $10^{-3}\varepsilon$	Solvent 0·01N in NaOH: H·CO·NMe_2 λ	Solvent 0·01N in NaOH: H·CO·NMe_2 $10^{-3}\varepsilon$	$-pK_a'$	Ref. (see p. 2616)
67	Me·CH:CH·CH:CH·COMe	390	36·5	6	480	30·5	496	38	3·0	*u*
16	Me_2C:CH·CH:CH·COMe	392	36	—	478	33	—	—	—	*v*
68	Me·CH:CMe·CH:CH·$COBu^t$	371	24	—	—	—	502	24·5	—	*u*
69	4-(2 : 6 : 6-Trimethyl*cyclo*hex-1-enyl)but-3-en-2-one	384	29·5	—	468	28	—	—	—	3
70	2-(1 : 3-Dimethylbut-2-enylidene)*cyclo*hexanone	406	26·5	—	476	26	—	—	—	*w*
71	2-(2-*cyclo*Hexylidene-ethylidene)*cyclo*hexanone	408	22	—	464	21·5	—	—	—	*x*
72	CH_2:CH·CMe:CH·CH:CH·COMe	398	38·5	—	497	35·5	—	—	—	*y*
18	Retinene$_1$	437	59·5	7	518	62·5	548	61·5	3·4	*z*
73	Ph·CHO	379	28	−4	464	30	488	34·5	3·3	*g*
19	Ph·COMe	376	26	—	460	24	482	30	—	*g*
74	Ph·$COBu^t$	376	26	—	463	22·5	—	—	—	*aa*
75	*p*-MeO·C_6H_4·CHO	390	25	—	466	26·5	—	—	—	*g*
76	3 : 4 : 1-MeO·C_6H_3(OH)·CHO	393	27	—	478	27·5	—	—	—	*g*
77	Furfuraldehyde (m. p. 223—225°)	388	26	1	470	30·5	—	—	3·7	*bb*
78	Furfuraldehyde (m. p. 194—196°)	375	28	5	476	28·5	—	—	3·2	*bb*
79	Ph·CH:CH·CHO	391	37	−1	488	41·5	508	44	3·5	*r*
80	Ph·CH:CMe·CHO	384	36·5	—	470	36·5	—	—	—	*r*
81	Ph_2C:CMe·CHO	386	36	—	478	36·5	—	—	—	*r*
20	Ph·CH:CH·COMe	391	35	—	488	34	508	42	—	*r*
82	4-Methyl-3-phenyl*cyclo*hex-2-enone	389	33·5	—	480	31	—	—	—	*cc*
83	1-Cinnamylidene-6 : 6 : 10-trimethyl-2-decalone	412	27	8	488	24	—	—	—	*t*
84	1-(*cyclo*Hexylideneacetyl)*cyclo*hexene (m. p. 150—155°)	373	25	6	—	—	464	23·5	2·5	*dd*
85	Di(*cyclo*hex-1-enyl) ketone	380	27·5	—	—	—	476	28	—	*ee*
15	Me_2C:CH·CO·CH:CMe_2	386	26·5	10	—	—	492	28·5	1·3	*ff*
86	Ph·CO·CH:CH_2	378	24	—	458	20·5	—	—	—	*r*
87	Ph_2CO	379	29	8	—	—	502	32	2·0	*r*
88	Ph·C:C·CO·CH:CHPh	397	37·5	—	510	~31 *	—	—	—	*r*
89	Ph·C:C·COPh	390	30·5	—	498	~21 *	—	—	—	*r*
90	3-Cyano-2-phenylinden-1-one	*375*	*9*	—	—	—	*535*	*15*	—	*gg*
		430	28·5	0	—	—	594	66·5	4·3	
91	3-Carbamoyl-2-phenylinden-1-one	387	27 †	—	—	—	*501*	*13*	—	*gg*
		432	*20* †	—	—	—	576	50·5	—	

	Polycarbonyl compounds	Neutral solvents: 10% $CHCl_3$ in EtOH	Neutral solvents: H·CO·NMe_2		Solvents 0·01N in NaOH: 10% $CHCl_3$ in EtOH	Solvents 0·01N in NaOH: H·CO·NMe_2			$-pK_a'$	Ref.
	Mono-derivatives									
92	Me·CO·COPr	351	16·5	—	—	500	23·5	—	—	—	*hh*
22	Et·CO·COPr	351	23·5	—	—	512	34	—	—	—	
93	2-Methylnaphtha-1 : 4-quinone	457	38	460	42	635	70	635	83	4·1	*ii*
	Bis-derivatives :									
94	OHC·CHO	—	—	*385*	*20·5*	—	—	588	59	—	*jj*
				448	42·5						
95	Me·CO·COMe	—	—	412	38	—	—	572	48·5	—	*c*
				478	*20·5*						
23	Et·CO·COPr	392	38	409	40·5	558	44·5	570	34	—	10
		451	*28*	*472*	*24·5*						
96	3 : 4 : 1-MeO·C_6H_3(OEt)·CO·COMe	399	43	413	47	556	49	576	59·5	3·7	*kk*
		458	*23·5*								

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classes, hydroxylic, non-hydroxylic, and a third group giving much larger bathochromic shifts. Within each class the position of the absorption maximum increases with increasing dielectric constant of the solvent. In benzonitrile an exceptionally large bathochromic shift is observed

Simple alkyl substitution produces bathochromic shifts (see, *e.g.*, nos. 24, 25, 12, and 34) but in more complex examples hypsochromic shifts are found (*e.g.*, nos. 38 and 39; 73 and 19; 79 and 80) particularly when the substituent is near the dinitrophenylhydrazone residue. Hydroxy- and alkoxy-substituents give variously both bathochromic and hypsochromic shifts, probably depending on the configuration of the derivative (cf., *e.g.*, nos. 44 and 45). Several pairs of derivatives from particular carbonyl compounds have been studied; in some cases they have different spectra (*e.g.*, nos. 44 and 45; 77 and 78) but in the absence of substituents other than alkyl, no appreciable differences in spectra were observed (*e.g.*, nos. 25 and 11; 30 and 31).

The bis-derivatives of α-dicarbonyl compounds are distinguished by the increased intensities of the E_2 and more particularly of the B bands. With the glyoxal derivative (no. 94), the B band is the most intense, but alkyl substitution enhances the E_2 band relatively to the B band (cf., *e.g.*, nos. 95 and 23).

Alkaline Solutions.—In the presence of alkali the four bands are all shifted towards longer wavelengths in both the 2 : 4-dinitrophenylhydrazones and related aromatic compounds (Table 1). By analogy with the bands in neutral solutions, the first three bands will be termed E_0^-, E_1^-, and E_2^- bands. The longest-wavelength band for reasons stated in the discussion is called the NO_2^- band. For most derivatives the solvent mixture, 10%(v/v) $CHCl_3$ in EtOH, is suitable; the alkali bands were fully produced by addition of aqueous sodium hydroxide to make the solutions N/100 in sodium hydroxide. With less soluble compounds (*e.g.*, bis-derivatives) and with less acidic derivatives (*e.g.*, no. 15) N/100-alkali in dimethylformamide was necessary, the latter being a more powerful solvent and having greater ionising properties.[16] For comparison of derivatives in either solvent a number of spectra are recorded in Table 2 in both solvents.

The NO_2^- band is resolved as a discrete but broad band with derivatives of saturated aldehydes and ketones and is of value for distinguishing the two (498—512 mμ for aldehydes and 515—540 mμ for ketones in 10% $CHCl_3$–EtOH). Of more general application is the E_2^- band, the wavelength of which increases with increasing number of conjugated double bonds in the carbonyl compound. Whilst a linear relation between the square of the wavelength and the number of double bonds holds up to $n = 3$, the curve then starts to converge with the compounds studied (Fig. 1). An acetylenic bond gives a smaller increment than an ethylenic bond as in the spectra of the neutral derivatives [17] (*e.g.*, 13). Phenyl groups are equivalent to about 1·2 double bonds. The derivatives of cross-conjugated ketones absorb at shorter wavelengths than those of comparable linear conjugated ketones (cf. nos. 15 and 67) in the same solvent. Saturated substituents produce only small effects on the spectra of the ions, so that the spectra in alkaline solution are more characteristic of the extent of conjugation than the spectra in neutral solution. In contrast, substituents which can readily accommodate a negative charge (*e.g.*, C=O) produce large bathochromic shifts with the ions, but only small changes with the neutral molecules (*e.g.*, nos. 22, 23, 92—96). Hypsochromic shifts resulting from steric hindrance by substituents are less pronounced in the spectra of the ions than of the neutral molecules when the steric hindrance is small (cf., *e.g.*, nos. 59, 60), but larger shifts are found in alkaline than in neutral solution when the hindrance is great (*e.g.*, no. 69).

Qualitatively the colour in alkaline solution gives a rough indication of the extent of the conjugation present, although it is now apparent that a blue colour is not specific [11] for bis-derivatives of α-diketones, but is shown by all derivatives giving particularly stable anions (*e.g.*, nos. 90, 91, and 93).

[16] Porter, *Analyt. Chem.*, 1955, **27**, 805.
[17] Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, **39**.

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Acid Strengths.—A large variation in the acid strengths, conveniently measured spectrophotometrically, was encountered (pK_a varying from −1·3 to −3·4; see Table 2). Particularly weak acids were the derivatives of cross-conjugated ketones and sterically hindered ketones.

Preparation of 2 : 4-Dinitrophenylhydrazones.—Most of the derivatives studied had been prepared earlier for other work. The new compounds, described in detail in the Experimental section, include examples of acid-sensitive compounds (nos. 62, 63, 64) which were conveniently prepared in pyridine solution.[18]

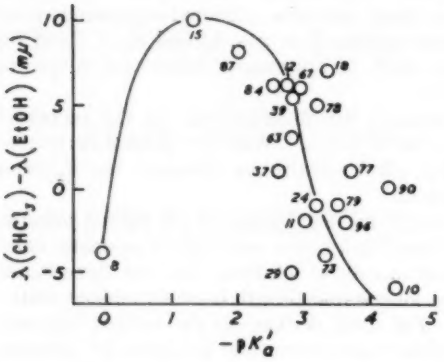


FIG. 3. *Plot of solvent shifts of main bands of various 2 : 4-dinitrophenylhydrazones and related compounds against apparent pK_a' values.*

DISCUSSION

Neutral Solvents.—In the absence of hydrogen bonding, λ($CHCl_3$) − λ(EtOH) would be expected to be negative, on account of the larger dielectric constant of ethanol. This is found with 2 : 4-dinitroaniline (no. 8) (Fig. 3) which is a very weak acid so that the amino-hydrogen atom is not available for hydrogen bonding. With stronger acids such as 2 : 4-dinitrophenylacethydrazide (no. 10), an internal hydrogen bond is present: since it is present in both solvents, λ($CHCl_3$) − λ(EtOH) is also negative. With intermediate acid strengths external hydrogen bonding with the solvent and internal bonding are both possible. The ratio of the two will be influenced by several factors, such as the extent of conjugation and steric effects in these 2 : 4-dinitrophenylhydrazones. Thus there is little correlation between solvent shifts and acid strengths, when pK' is between −2·6 and −3·4, as shown in Fig. 3. However, in general, at acid strengths greater than pK_a' −1·2, as the acidity of the amino-hydrogen increases, the value of λ($CHCl_3$) − λ(EtOH) decreases. The different behaviour of acetone *p*-nitrophenylhydrazone (no. 6) (see p. 2616) confirms that the internal hydrogen bonding involves the *o*-nitro-group.

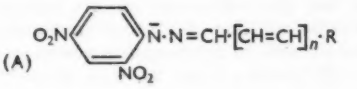
The group of solvents giving the bathochromic solvent shifts out of proportion to their dielectric constant is unexpected, but these shifts probably arise from π-complex formation between the solvent and solute.[19] In the polyene field the hitherto unexplained bathochromic solvent effects with carbon disulphide [20] may be attributed to the same cause.

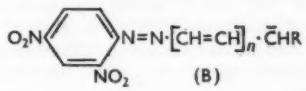
Alkaline Solutions.—That dinitrophenylhydrazones ionise by loss of a proton from the amino-nitrogen atom [14] is shown by the stability of the *N*-alkyl derivatives [21] to alkali.[6] Thus light absorption by dinitrophenylhydrazones in alkaline solution involves the ion (A) and other canonical forms such as (B), (C), and (D).

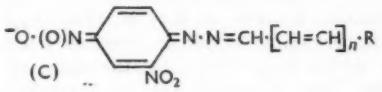
The E_2^- and NO_2^- bands may be ascribed to two separate transitions: the E_2^- band to a transition of the type C ⟷ A ⟷ B, and the NO_2^- band to a transition of the type C ⟷ D. The latter would be expected to give the longer-wavelength band, when *n* is

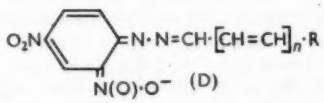
[18] Table 2, Refs. *c* and *g*.
[19] For review see Orgel, *Quart. Rev.*, 1954, **8**, 422.
[20] Karrer and Jucker, "Carotenoids," Elsevier, Amsterdam, 1950.
[21] Ragno, *Gazzetta*, 1945, **75**, 193, 200.

small, because the energy difference between (C) and (D), with a negative charge readily accommodated on any one of the four oxygen atoms, will be only the difference between the *o*- and *p*-quinonoid resonance energies, which will be smaller than the difference in energy between forms such as (B) and (C) where the negative charge is accommodated on the less electronegative carbon atom. Support for this assignment of the long-wavelength band is provided by the spectra in alkali of various 2 : 4-dinitrobenzene derivatives [16] (Table 1) which show bands of comparable intensities in the 500 mμ region, almost independently of the substituent in the 1-position provided it allows the formation of the ion.

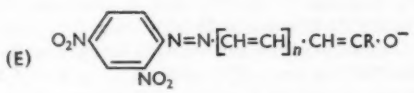

(A)

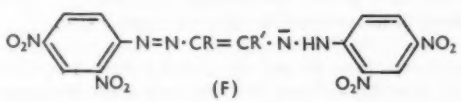

(B)

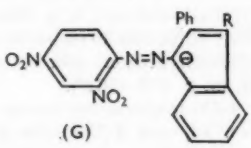

(C)


(D)

The E_2^- band is of interest as it appears to be the first example studied in detail of charge-resonance spectra in a vinylogous series of anions, although numerous cationic series have been investigated.[22,23] Isolated examples of charge-resonance spectra involving vinylogous anions reported include 1 : 3-diketones, glutaconic derivatives and its vinylogues,[24] and the oxonols.[25] With the dinitrophenylhydrazone anions the convergence of wavelength of the maxima with increase of n is expected for a series in which the two extreme structures, *i.e.*, B and C, have different energies.[23]


(E)


(F)


(G)

Saturated substituents have little effect, since both ground and excited states are ionic, and will be affected similarly, so that the energy difference between the two states is unchanged, in contrast to the greater effect with the neutral molecules where only the excited state is ionic. Covalently unsaturated substituents may provide an alternative extreme structure, *e.g.*, (E), the energy of which will be lowered with respect to (B) by accommodation of the charge on the more electronegative oxygen instead of on a carbon atom. With bis-derivatives of α-dicarbonyl compounds similar but greater bathochromic shifts arise from contributions of structures such as (F). In the indenone derivatives (nos. 90 and 91), the high-intensity long-wavelength band results from the high stability [26] of the substituted *cyclo*pentadienyl anion (G).

[22] Thomas and Branch, *J. Amer. Chem. Soc.*, 1953, **75**, 4793; Fisher and Hamer, *Proc. Roy. Soc.*, 1936, *A*, **154**, 703; Beilenson, Fisher, and Hamer, *ibid.*, 1937, *A*, **163**, 138; Wizinger and Sontag, *Helv. Chim. Acta*, 1955, **38**, 363; Wizinger and Kölliker, *ibid.*, p. 372.

[23] Brooker and his co-workers, *Rev. Mod. Phys.*, 1942, **14**, 275, and numerous later papers; Herzfeld and Sklar, *ibid.*, p. 294.

[24] Schwarzenbach, Lutz, and Felder, *Helv. Chim. Acta*, 1944, **27**, 576; Bateman and Koch, *J.*, 1945, 216; Stobbe and Wildensee, *J. prakt. Chem.*, 1927, **115**, 163.

[25] Sveschnikov and Levkoev, *Zhur. obshchei Khim.*, 1940, **10**, 274; Hamer and Winton, *J.*, 1949, 1126; Knott, *J.*, 1952, 2399.

[26] Armit and Robinson, *J.*, 1922, 827; 1925, 1604; E. Hückel, "Grundzüge der Theorie ungesättigter und aromatischer Verbindungen," Verlag Chemie, Berlin, 1938, p. 71.

XUM

Experimental

Heptane-3 : 4-dione 2 - 4-Dinitrophenylhydrazone (*no.* 22).—This compound was originally assigned the alternative structure 4-hydroxyhept-5-en-3-one 2 : 4-dinitrophenylhydrazone,[10] but the present spectroscopic results indicate the correct structure.

2 : 4-*Dinitrophenylhydrazone* of *Pyran-2-aldehyde* (*no.* 33).—This compound was obtained by Owen and Peto,[27] who suggested alternative structures. The above constitution was later suggested by Professor D. H. R. Barton [28] and is supported by the light absorption.

2 : 4-*Dinitrophenylhydrazones of* βγγ-*Trimethylvaleraldehyde* (*no.* 27), 5 : 5-*dimethylhex-3-en-2-one* (*no.* 55) *and* 2 : 2-*dimethylhex-4-en-3-one* (*no.* 59).—Reaction of *tert.*-butylmagnesium chloride with crotonaldehyde in ether,[29] followed by addition of aqueous ammonium chloride solution and ether-extraction, afforded a mixture which on fractionation gave βγγ-trimethylvaleraldehyde (40%), b. p. 96—101°/114 mm., n_D^{25} 1·4260 (cf. ref. 29, b. p. 56—57°/19 mm.), $\lambda_{max.}$ 280 and 290 mμ (ε 17, ε 17, in hexane) [2 : 4-*dinitrophenylhydrazone* (no. 27), m. p. 96—98°, light orange needles from methanol (Found: C, 54·9; H, 6·7; N, 17·6. $C_{14}H_{20}O_4N_4$ requires C, 54·9; H, 6·6; N, 17·6%)], and higher-boiling material. Further fractionation of the latter gave 2 : 2-dimethylhex-4-en-3-ol (15%), b. p. 110—114°/183 mm., n_D^{20} 1·4418 (cf. ref. 29, b. p. 75—76°/36 mm., n_D^{25} 1·4369). The 3 : 5-*dinitrobenzoate* crystallised from aqueous ethanol with m. p. 92—94° (Found: C, 55·6; H, 5·7; N, 9·2. $C_{15}H_{18}O_6N_2$ requires C, 55·9; H, 5·6; N, 8·7%). The 2 : 4-*dinitrophenylhydrazone* (no. 59) of 2 : 2-dimethylhex-4-en-3-one was formed directly from the unsaturated alcohol [30] in the cold and crystallised from methanol in orange needles, m. p. 132—136° (Found: C, 55·3; H, 6·1; N, 18·0. $C_{14}H_{18}O_4N_4$ requires C, 54·9; H, 5·9; N, 18·3%).

When the products from the Grignard reaction were washed in ether with aqueous sodium hydrogen sulphite, fractionation gave also the rearrangement product 5 : 5-*dimethylhex-3-en-2-ol*, b. p. 91—93°/52 mm., n_D^{23} 1·4360 (Found: C, 75·2; H, 12·6. $C_8H_{16}O$ requires C, 75·0; H, 12·6%), the 3 : 5-*dinitrobenzoate* of which crystallised from methanol with m. p. 130—134° (Found: N, 9·3. $C_{15}H_{18}O_6N_2$ requires N, 8·7%), and 5 : 5-*dimethylhexa-1 : 3-diene*, b. p. 41°/52 mm., n_D^{23} 1·4411, $\lambda_{max.}$ in EtOH 224 mμ (ε 25,000) (Found: C, 86·5; H, 13·1. C_8H_{14} requires C, 87·2; H, 12·8%). Oxidation of the alcohol with manganese dioxide [31] gave 5 : 5-dimethylhex-3-en-2-one, b. p. 99—105°/74 mm., n_D^{26} 1·4380, $\lambda_{max.}$ in EtOH 218, 234, and 314 mμ (ε 10,000, 9000, and 30 respectively) (cf. ref. 32, b. p. 78—80°/40 mm., n_D^{20} 1·4430). The 2 : 4-dinitrophenylhydrazone (no. 55) crystallised from ethanol in light red needles, m. p. 175° (cf. ref. 32, m. p. 159—161°).

2 : 4-*Dinitrophenylhydrazones of* 3-*Hydroxy-* (*nos.* 40 *and* 41) *and* 3-*Ethoxy-3-methylbutan-2-one* (*no.* 46) *and* 3-*Methylbut-3-en-2-one* (*no.* 53).—From 3-hydroxy-3-methylbutan-2-one in ethanol was obtained a mixture which was separated by chromatography into the *derivatives* of 3-ethoxy-3-methylbutan-2-one (no. 46), yellow needles (from methanol), m. p. 113—114° (Found: C, 50·1; H, 5·8; N, 18·3; OEt, 11·3. $C_{13}H_{18}O_5N_4$ requires C, 50·3; H, 5·8; N, 18·1; OEt, 14·5%), and of 3-methylbut-3-en-2-one (no. 53), m. p. 194—195° (cf. ref. 33, m. p. 192°). The latter was undepressed on admixture with a sample, kindly provided by Dr. N. Thorne, reported [34] as the derivative of 3-hydroxy-3-methylbutan-2-one. The revised structure is confirmed by the light absorption, behaviour on paper chromatography, and analysis (Found: C, 50·2; H, 4·5; N, 20·6. Calc. for $C_{11}H_{12}O_4N_4$: C, 50·0; H, 4·6; N, 21·2%).

From 3-hydroxy-3-methylbutan-2-one in water was obtained the corresponding 2 : 4-dinitrophenylhydrazone (no. 41), m. p. 145—147° after chromatography on alumina and crystallisation successively from benzene–light petroleum (b. p. 60—80°) and aqueous methanol (cf. ref. 35, m. p. 148°). The isomeric derivative (no. 40), unaffected by crystallisation from aqueous methanol, was converted into the high-melting derivative (no. 41) by chromatography on alumina.

[27] Owen and Peto, *J.*, 1956, 1146.
[28] Barton, personal communication to Dr. L. N. Owen.
[29] Stevens, *J. Amer. Chem. Soc.*, 1935, **57**, 1112.
[30] Braude and Forbes, *J.*, 1951, 1762.
[31] Cf. Weedon, *Ann. Reports*, 1953, **50**, 169.
[32] Campbell, *J. Amer. Chem. Soc.*, 1937, **59**, 1980.
[33] Table 2, ref. *n*.
[34] Thorne, *J.*, 1956, 2587.
[35] Table 2, ref. i.

XUM

2 : 4-*Dinitrophenylhydrazone of* 2 : 5-*Dimethylhex-4-en-3-one* (*no.* 60).—*iso*Butyroin [10] (10 g.) and phosphorus oxychloride (5 g.) were heated in pyridine (20 ml.) for 3 hr. on the steam-bath. The cold, partly solidified product was dissolved in pentane and washed successively with dilute hydrochloric acid and sodium hydrogen carbonate solution. Distillation of the dried (Na_2CO_3) pentane solution afforded crude 4-chloro-2 : 5-dimethylhexan-3-one (2·5 g.) which with 2 : 4-dinitrophenylhydrazine in boiling glacial acetic acid [36] afforded the *derivative* (no. 60) of 2 : 5-dimethylhex-4-en-3-one which crystallised from hexane in orange leaves, m. p. 115—116° (Found: C, 54·6; H, 6·0; N, 18·1. $C_{14}H_{18}O_4N_4$ requires C, 54·9; H, 5·9; N, 18·3%).

2 : 4-*Dinitrophenylhydrazones of* 3-*Methoxybut-3-en-2-one* (*nos.* 62 *and* 63).—3 : 3-Dimethoxybutan-2-one [37] (1 g.) and 2 : 4-dinitrophenylhydrazine (2 g.) in pyridine [18] (10 ml.) were heated almost to the b. p. for several minutes. The product, on dilution with benzene and chromatography on alumina, afforded the isomeric *derivatives* of 3-methoxybut-3-en-2-one, m. p. 173—175° (no. 62), which crystallised from benzene–hexane in orange needles (0·25 g.) (Found: C, 47·6; H, 4·4; N, 19·9. $C_{11}H_{12}O_5N_4$ requires C, 47·2; H, 4·3; N, 20·0%), and m. p. 147—149° (no. 63), which crystallised from the mother-liquors in orange prisms (0·30 g.) (Found: C, 47·3; H, 4·5; N, 20·7%).

2 : 4-*Dinitrophenylhydrazone of* 3-iso*Propoxyhex-2-enone* (*no.* 64).—This *derivative*, prepared in pyridine as above from 3-*iso*propoxyhex-2-enone, crystallised from benzene–light petroleum (b. p. 40—60°) in crimson needles, m. p. 151—152° (Found: C, 54·3; H, 5·4; N, 16·5; OPr^i, 19·1. $C_{15}H_{18}O_5N_4$ requires C, 53·9; H, 5·4; N, 16·8; OPr^i, 17·7%).

Spectroscopic Measurements.—The spectra were determined by Miss D. Green using a Unicam S.P.500 spectrophotometer. Dimethylformamide was purified by drying over CaO and vacuum-distillation. Any resulting excess of base was neutralised by addition of 98—100% formic acid. Small amounts of acidic and basic impurities were determined by titration with aqueous standard acid and alkali, the bis-2 : 4-dinitrophenylhydrazone of diacetyl (no. 95) being used as indicator. The dimethylformamide used for determining the spectra of the un-ionised molecules was between 0·01N and 0·005N in formic acid. Submerged bands were resolved graphically, by assuming that the resolved bands were symmetrical about their maximum on a wavelength scale. The components were then evaluated so that their summation fitted the experimental absorption curve. The apparent pK_a' values in 10% v/v chloroform–ethanol were obtained graphically by plotting the extinction coefficient at the wavelength of the E_2^- (or in some cases the NO_2^-) band maximum against alkali concentration and taking the pK_a' value as equal to the logarithm of the alkali concentration when equal amounts of ionised and un-ionised dinitrophenylhydrazone were present.

We thank numerous colleagues who generously made samples of 2 : 4-dinitrophenylhydrazones available for this work, particularly the late Professor E. A. Braude (nos. 70, 71, 84, and 85), Dr. L. Crombie (no. 13), Dr. W. J. Hickinbottom (no. 41), Dr. L. N. Owen (no. 33), Dr. H. J. Vipond (no. 57), Dr. B. C. L. Weedon (nos. 66—68, 72) and Dr. K. R. H. Wooldridge (nos. 20, 30, 31, 58, 79—82, 86—89).

THE UNIVERSITY, NOTTINGHAM. [*Received, December 27th,* 1956.]

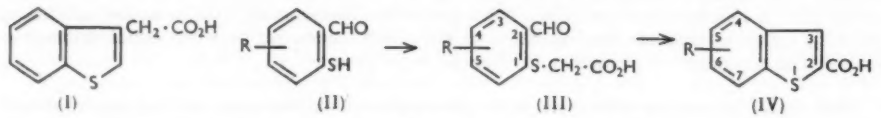
[36] Djerassi, *J. Amer. Chem. Soc.*, 1949, **71**, 1003.
[37] Table 2, ref. *c*.

509. *Thionaphthencarboxylic Acids.*

By G. M. Badger, D. J. Clark, W. Davies, K. T. H. Farrer, and N. P. Kefford.

All the isomeric thionaphthencarboxylic acids, except thionaphthen-4-carboxylic acid, have been synthesised. Most of these syntheses involve intermediate formation of bromothioindoxyls by ring closure from the appropriate *ortho*-substituted (bromophenylthio)acetic acids. Ring closure was facilitated by the presence of a formyl group or its equivalent in the *ortho*-position to a carboxyl or cyano-group.

Since 3-thionaphthenylacetic acid [1] (I) has growth-promoting action on plants, attempts, interrupted by the war, have been made to prepare and test biologically all of the possible thionaphthenylacetic acids. This has been done,[2] with the exception of 4-thionaphthenylacetic acid which has been made otherwise,[3] by preparing the corresponding thionaphthencarboxylic acids (by carboxylation of the thionaphthenyl Grignard reagents) and converting these, through their diazo-ketone derivatives, into the thionaphthenylacetic acids. The Grignard process was unsuccessful with 4-bromothionaphthen, and thionaphthen-4-carboxylic acid is still unknown. The required bromothionaphthens were obtained by reduction of the corresponding thioindoxyls produced by cyclisation of (bromophenylthio)-acetic, (bromo-2-carboxyphenylthio)acetic, or (bromo-2-cyanophenylthio)acetic acids. Although there is no ambiguity in the structure of the thionaphthens made from the corresponding thioindoxyls, the yields can be very low, for reasons given by Banfield *et al.*[4] Intermediate formation of thioindoxyls was sometimes avoided by cyclising (unisolated) (*o*-formylphenylthio)acetic acids (III) or their aldimine equivalents, to give the acids (IV). It is now found that thiosalicylaldehyde (II; R = H) can be made directly in very small yield by the reduction of thiosalicylic or dithiosalicylic acid with sodium amalgam, analogously to the conversion of salicylic acid into salicylaldehyde by Weil.[5] Attention



is directed to the good yield [6] of thiosalicylaldehyde obtained by the reduction of *N*-methylthiosalicylanilide with lithium aluminium hydride. Another useful innovation is the application of Stephen's method [7] for the reduction of (*o*-cyanophenylthio)acetic acid (X; R = H) to the aldehydic acid (XI; R = H) or the corresponding imidoyl chloride. Although, because of steric hindrance, this method fails with some *ortho*-derivatives of benzonitrile,[8,9] useful yields of thionaphthen-2-carboxylic acid and 5-bromothionaphthen-2-carboxylic acid have been obtained.

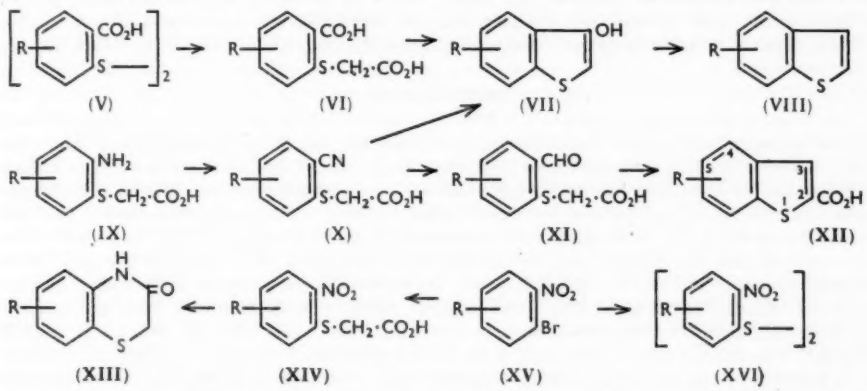
Hartough and Meisel,[9] referring to the contrast in the m. p. 114° of the thionaphthen-2-carboxylic acid obtained by the cyclisation of (*o*-formylphenylthio)acetic acid [10] (III; R = H) and m. p. 236° of the acid obtained by metallation of thionaphthen followed by

[1] Crook and Davies, *J.*, 1937, 1697; Blicke and Sheets, *J. Amer. Chem. Soc.*, 1948, **70**, 3768; Steinkopf, "Die Chemie des Thiophens," Steinkopff, Leipzig, 1941, p. 164.
[2] Kefford and Kelso, *Austral. J. Biol. Sci.*, 1957, **10**, 80.
[3] Kloetzel, Little, and Frisch, *J. Org. Chem.*, 1953, **18**, 1511.
[4] Banfield, Davies, Ennis, Middleton, and Porter, *J.*, 1956, 2603.
[5] Weil, *Ber.*, 1908, **41**, 4147.
[6] Weygand and Eberhardt, *Angew. Chem.*, 1953, **65**, 525.
[7] Stephen, *J.*, 1925, **127**, 1874.
[8] *Idem*, *J.*, 1930, 2786; King, L'Ecuyer, and Openshaw, *J.*, 1936, 352.
[9] Hartough and Meisel, "Compounds with Condensed Thiophene Rings," Interscience Publ. Inc., New York, 1954, p. 131.
[10] Friedländer and Lenk, *Ber.*, 1912, **45**, 2083.

carboxylation,[11] suggest that the lower melting point (114°) " indicated impurity." Both of these syntheses have been repeated and thionaphthen-2-carboxylic acid is also made by the removal of the nitro-group after cyclisation of (5-nitro-2-formylphenylthio)acetic acid (III; R = 5-NO_2). In all three cases the acids had m. p. and mixed m. p. 236°. Additional evidence in favour of structure (IV; R = H) for this acid is obtained by a consideration of the different syntheses of thionaphthen-2 : 3-dicarboxylic acid. This acid is now obtained by the action of ethylmagnesium iodide and carbon dioxide on 3-bromothionaphthen, on thionaphthen-3-carboxylic acid, and on thionaphthen, and also from thionaphthen-2 : 3-quinone by repeating the method of Bezdrik, Friedländer, and Koeniger.[12] Finally, as the thionaphthen-2-carboxylic acid (m. p. 236°) was desulphurised by Blicke and Sheets [1] to the expected β-phenylpropionic acid, the m. p. 114° recorded for the acid may be due to a clerical error.

Crook and Davies [1] ascribe m. p. 174—175° to thionaphthen-3-carboxylic acid, and also describe a thionaphthenylidenediacetic acid, m. p. " about 108°." This is a clerical error for " about 208°," and the compound is probably 2 : 3-thionaphthenylenediacetic acid.

Thionaphthen-5-carboxylic acid (VIII; R = 5-CO_2H) was synthesised by carboxylation of the Grignard complex from 5-bromothionaphthen, prepared by Clemmensen reduction of 5-bromothioindoxyl. Since this method can cause some reduction of the thiophen ring and even loss of bromine, a gentler reduction with " mossy zinc " (see p. 2628) was found advisable, though even with this modification the yields of bromothionaphthen were poor. A more direct synthesis is by the decarboxylation of 5-bromothio-



naphthen-2-carboxylic acid (XII; R = 5-Br), formed by cyclisation of (unisolated) (4-bromo-2-formylphenylthio)acetic acid (XI; R = 4-Br) or its equivalent, arising from reduction of the cyano-group in (4-bromo-2-cyanophenylthio)acetic acid (X; R = 4-Br).

The preparation of 5-bromothioindoxyl by cyclisation of (*p*-bromophenylthio)acetic acid [13] is inferior to cyclisation with acetic anhydride of (4-bromo-2-carboxyphenylthio)-acetic acid (VI; R = 4-Br), readily made from 4 : 4'-dibromodithiosalicylic acid (V; R = 4-Br) by reduction and interaction with chloroacetic acid. A better method is to start with 2 : 5-dibromonitrobenzene (XV; R = 5-Br) which with sodium disulphide gives the disulphide (XVI; R = 4-Br), easily converted into (4-bromo-2-nitrophenylthio)acetic acid (XIV; R = 4-Br); this was made in higher yield (90%) by direct interaction of the bromide (XV; R = 4-Br) with mercaptoacetic acid. Reduction of this nitro-acid gave 6-bromo-3 : 4-dihydro-3-oxo-1 : 4-benzothiazine (XIII; R = 6-Br) (also directly obtained from 4-bromo-2-nitroaniline by diazotisation and then condensation with chloroacetic

[11] Weissberger and Kruber, *Ber.*, 1920, **53**, 1561.
[12] Bezdrik, Friedländer, and Koeniger, *Ber.*, 1908, **41**, 227.
[13] Pummerer, *Ber.*, 1909, **42**, 2279.

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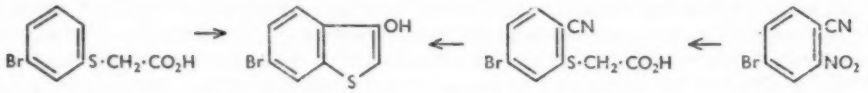
acid and sodium disulphide, the last named reagent reducing the nitro-group). A Sandmeyer reaction on the (2-amino-4-bromophenylthio)acetic acid from this benzothiazine gave (4-bromo-2-cyanophenylthio)acetic acid (X; R = 4-Br) which, with alkali followed by acid, formed 5-bromothioindoxyl (VII; R = 5-Br).

For preparation of thionaphthen-6-carboxylic acid (VIII; R = 6-CO_2H) 6-bromothioindoxyl was obtained by cyclisation of (*m*-bromophenylthio)acetic acid. The product was identical with that synthesised unambiguously from 4-bromo-2-nitroaniline, produced by the nitration of *p*-bromoacetanilide, followed by hydrolysis, as described by Hübner.[14] In this nitration difficulty was encountered in preventing migration of the bromo-substituent,[15] so *o*-nitroaniline was brominated to give 4-bromo-2-nitroaniline,[16] which was converted into 4-bromo-2-nitrobenzonitrile (XX). Holmes and Loudon [17] have shown that the nitro-group in the analogous 4-chloro-2-nitrobenzonitrile is mobile, and similar mobility occurs with the bromo-compound, for (5-bromo-2-cyanophenylthio)acetic acid (XIX) was easily obtained from it. The above acid was then converted into 6-bromothioindoxyl (XVIII) which was reduced to 6-bromothionaphthen (VII; R = 6-Br).



(XVII) (XVIII) (XIX) (XX)

Thioindoxyl-7-carboxylic acid was obtained by cyclisation of (*o*-carboxyphenylthio)-acetyl chloride with aluminium chloride in *o*-dichlorobenzene. The yield was good and reduction in the usual way gave thionaphthen-7-carboxylic acid (VIII; R = 7-CO_2H).

Experimental

(*o-Cyanophenylthio*)*acetic Acid* (X; R = H).—*o*-Nitrochlorobenzene was converted into di-(*o*-nitrophenyl) disulphide [18] and thence by Claaz's method [19] into (*o*-nitrophenylthio)acetic acid; however, the last compound was more easily prepared by the direct reaction [20] of *o*-chloronitrobenzene with mercaptoacetic acid, as follows. *o*-Chloronitrobenzene (31·5 g.), mercaptoacetic acid (15·2 ml.), and sodium hydrogen carbonate (40 g.) in 50% aqueous alcohol (440 ml.) were refluxed for 3 hr. The alcohol was evaporated and the residue diluted with hot water. The cold solution was filtered and the filtrate on acidification gave a precipitate of (*o*-nitrophenylthio)acetic acid (XIV; R = H) which crystallised from water as light yellow needles, m. p. 164° (Claaz [19] gives m. p. 163—164°) (23·5 g.; 55%). Reduction with hydrogen sulphide and ammonia gave 3 : 4-dihydro-3-oxo-1 : 4-benzothiazine (XIII; R = H) (85%), m. p. 179° (Unger,[21] who treated bromoacetic acid with *o*-aminothiophenol, gives m. p. 179°).

A mixture of this dihydro-oxobenzothiazine (10 g.) and sodium hydroxide (12 g.) in water (50 ml.) was boiled for ½ hr. After cooling and dilution with twice its volume of ice, the solution was almost neutralised with concentrated hydrochloric acid, and sodium nitrite (6 g.) added. The solution was then added dropwise to a cold solution of concentrated hydrochloric acid (50 ml.) and water (50 ml.), neutralised (to Congo-red), and then added to an ice-cold solution of cuprocyanide complex from copper sulphate (15 g.) in water (80 ml.) with potassium cyanide (17 g.) in water (40 ml.). The cuprocyanide solution, which during the addition was kept at about pH 6, was gently heated after 1 hr. until effervescence ceased, cooled, made slightly acid to litmus with hydrochloric acid, filtered, and then strongly acidified. (*o*-Cyanophenylthio)-acetic acid (X; R = H) (6·5 g., 60%) formed light brown crystals (from water), m. p. 141° (lit., m. p. 140°, 142°).

Thionaphthen-2 : 3-*dicarboxylic Acid* (by Dr. E. M. Crook).—In preparing a relatively large

[14] Hübner, *Annalen*, 1881, **209**, 339.
[15] Cf. Griffith, *J.*, 1924, 940.
[16] Fuchs, *Monatsh.*, 1915, **36**, 139.
[17] Holmes and Loudon, *J.*, 1940, 1953.
[18] Bogert and Stull, *Org. Synth.*, Coll. Vol. I, 2nd Edn., 1944, p. 220.
[19] Claaz, *Ber.*, 1912, **45**, 2427.
[20] Friedländer and Chwala, *Monatsh.*, 1907, **28**, 250.
[21] Unger, *Ber.*, 1897, **30**, 607.

quantity of thionaphthen-3-carboxylic acid (from 10 g. of 3-bromothionaphthen) by the method of Crook and Davies [1] and prolonging the time of reaction, a benzene-insoluble acid (2 g.) was also obtained. After purification by sublimation, thionaphthen-2 : 3-dicarboxylic acid had m. p. 251° (Found : equiv., 113·5. Calc. for $C_{10}H_6O_4S$: equiv., 111). The anhydride, formed by prolonged heating with acetic anhydride, had m. p. 171°. The acid and the anhydride were identified by comparison with specimens prepared by Bezdrik, Friedländer, and Koeniger's method,[12] except that the intermediate thionaphthenquinone was made by the more convenient method of Pummerer.[22] Thionaphthen-2 : 3-dicarboxylic acid was also produced (in 10% yield) when thionaphthen-3-carboxylic acid, in ether, was heated with excess of ethyl iodide and magnesium, followed by carbon dioxide.

Thionaphthen-2-carboxylic Acid (XII; R = H).—(i) A solution of dithiosalicylic acid [23] (5 g.) and anhydrous sodium carbonate (1·8 g.) in boiling water (350 ml.) was treated with aniline (6 g.), then slowly cooled with stirring. Boric acid (5 g.), then 2% sodium amalgam (350 g.) were added with stirring during 1 hr., during which the solution was kept acid by the gradual addition of boric acid (100 g.). The red precipitate was filtered and steam-distilled from acid solution, and the distillate was run directly into an alkaline solution of sodium monochloroacetate (5 g.), which was then concentrated from 3 l. to 200 ml.; the filtered solution on acidification gave thionaphthen-2-carboxylic acid, m. p. 236° (0·5 g., 5%).

(ii) The difficulty in diazotising 5-aminothionaphthen-2-carboxylic acid (XII; R = 5-NH_2) made by the method of Fries *et al.*[24] is overcome by the following process (cf. Hodgson and Walker [25] and Hodgson and Turner [26]). Finely powdered sodium nitrite (1·87 g.) was stirred into concentrated sulphuric acid (12·4 ml.) at 0°. The temperature was raised to 70° until all the sodium nitrite had dissolved, and to the cold solution 5-aminothionaphthen-2-carboxylic acid (4 g.) in glacial acetic acid (35 ml.) was added, with stirring, at 0° during 30 min. The mixture was run into a stirred suspension of finely powdered cuprous oxide (5·8 g.) in absolute alcohol (50 ml.) during 30 min., the filtered precipitate was washed with alcohol, and the combined filtrates were concentrated and diluted with water. Thionaphthen-2-carboxylic acid (0·4 g., 11%) separated, having m. p. 236°, identical with the material obtained by the first method.

(iii) Dry hydrogen chloride was passed into a suspension of tin filings (2 g.) in anhydrous ether (10 ml.) until all had dissolved. (*o*-Cyanophenylthio)acetic acid (1 g.) in dry chloroform (15 ml.) was then added, and the solution saturated with hydrogen chloride, and then occasionally again so during a week. Then the solvent was distilled off and the residue refluxed with 18% hydrochloric acid solution (30 ml.) for 15 min., made alkaline, refluxed for 10 min., cooled, and acidified. It yielded to ether thionaphthen-2-carboxylic acid, m. p. 236° (0·2 g., 20%).

(*4-Bromo-2-carboxyphenylthio*)*acetic Acid* (VI; R = 4-Br).—Anthranilic acid (200 g.) in glacial acetic acid (1750 ml.) gave 5-bromoanthranilic acid (160 g.) when brominated essentially by the method of Wheeler and Oates; [27] this (50 g.) was diazotised and then reduced with sodium disulphide, to the dibromodithiosalicylic acid, m. p. 307° (40 g., 75%). This product was purer than that obtained (m. p. 291°) by brominating dithiosalicylic acid in acetic acid.

For the preparation of the thioacetic acid (VI; R = 4-Br), crude dibromodithiosalicylic acid (from 72 g. of 5-bromoanthranilic acid) was boiled in water (300 ml.) containing chloroacetic acid (37 g.) and sodium hydroxide (35 g.) for 2 hr. A further 12 g. of sodium hydroxide in a little water was added after a few minutes, and a similar quantity after the first hour.

(*4-Bromo-2-carboxyphenylthio*)*acetic acid* (VI; R = 4-Br) (65 g.), crystallised from water, has m. p. 215—217° (Found : equiv., 144. $C_9H_7O_4BrS$ requires equiv., 145·5). The same acid was obtained, in good yield, by interaction of chloroacetic acid in alkali with the 5-bromothiosalicylic acid made by the reduction of the dibromodithiosalicylic acid by zinc dust in acetic acid.

(*4-Bromo-2-nitrophenylthio*)*acetic acid* (XIV; R = 4-Br) was made from various starting materials. Interaction of 1 mol. of 5-bromo-2-chloronitrobenzene, 2 : 5-dibromonitrobenzene, or 5-bromo-2-iodonitrobenzene with 1 mol. of sodium disulphide in boiling alcohol for 2 hr. gave di-(4-bromo-2-nitrophenyl) disulphide (XVI; R = 4-Br) in 60, 65, and 80% yield respectively.

[22] Pummerer, *Ber.*, 1910, **43**, 1370.
[23] Allen and MacKay, *Org. Synth.*, Coll. Vol. II, 1944, p. 580.
[24] Fries, Heering, Hemmecke, and Siebert, *Annalen*, 1936, **527**, 83.
[25] Hodgson and Walker, *J.*, 1933, 1620.
[26] Hodgson and Turner, *J.*, 1942, 748.
[27] Wheeler and Oates, *J. Amer. Chem. Soc.*, 1910, **32**, 770.

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These yields were all higher than that obtained by the interaction of diazotised 4-bromo-2-nitroaniline with aqueous sodium disulphide. Claaz's method [19] for preparation of (arylthio)acetic acids from disulphides was used (55% yield) but a shorter reduction time with glucose was necessary to obtain a clean product. An excellent method, however, is from 2 : 5-dibromonitrobenzene as follows.

(i) A solution of 2 : 5-dibromonitrobenzene (120 g.), mercaptoacetic acid (44 g.), and sodium hydrogen carbonate (80 g.) in 3 : 1 aqueous alcohol (2·5 l.) was refluxed for 4 hr., evaporated to one-third of its volume, diluted with hot water (9 l.), filtered, and acidified giving (*4-bromo-2-nitrophenylthio*)*acetic acid* (XIV; R = 4-Br), yellow plates (from alcohol) (112 g., 90%), m. p. 218° (Found : C, 33·15; H, 2·35. $C_8H_6O_4NSBr$ requires C, 32·9; H, 2·05%).

6-Bromo-3 : 4-dihydro-3-oxo-1 : 4-benzothiazine (XIII; R = 6-Br).—(i) Hydrogen sulphide was passed into a mixture of powdered (4-bromo-2-nitrophenylthio)acetic acid (135 g.) and ammonia (*d* 0·95; 4100 ml.) during a week. All the powder disssolved to give a red solution. This solution was boiled for 4 hr., filtered hot, and acidified with excess of dilute sulphuric acid, a white precipitate being formed. When the mixture was warmed, the precipitate of *6-bromo-3 : 4-dihydro-3-oxo-1 : 4-benzothiazine* (80 g., 70%) coagulated, and was then crystallised from alcohol, forming needles, m. p. 206° (Found : C, 39·1; H, 2·7. C_8H_6ONSBr requires C, 39·35; H, 2·4%).

(ii) The most direct method, involving two reducing actions of sodium disulphide, is as follows. A solution of 4-bromo-2-nitroaniline (16 g.) in concentrated hydrochloric acid (200 ml.) was poured into water (200 ml.), cooled, and diazotised by sodium nitrite (5 g.) in water (20 ml.). The filtered diazo-solution was run slowly into alkaline sodium disulphide [from crystalline sodium sulphide (38 g.), sulphur (5 g.), sodium hydroxide (8 g.), and water (100 ml.)] at <5°, then after 1 hr. at room temperature the unstable disulphide was collected and immediately dissolved in sufficient aqueous alkali for the resulting solution to be about 2N with respect to sodium hydroxide. The mixture, with a neutralised solution of chloroacetic acid (7·5 g.) in water (50 ml.), was heated on the water-bath for 2 hr. and after acidification the precipitated 6-bromo-3 : 4-dihydro-3-oxobenzothiazine (6·2 g., 31%) was crystallised, forming needles (from alcohol), m. p. 206°. It was converted into (*4-bromo-2-cyanophenylthio*)*acetic acid* (6·5 g., 58%), m. p. 182—183° (from water) (Found : N, 5·2. $C_9H_6O_2SNBr$ requires N, 5·15%) in the same way that 3 : 4-dihydro-3-oxo-1 : 4-benzothiazine gave (*o*-cyanophenylthio)acetic acid (p. 2626).

5-Bromothioindoxyl (VII; R = 5-Br).—(i) (*p*-Bromophenylthio)acetic acid (1·3 g.) in hot dry benzene (15 ml.) was gradually treated with phosphorus pentoxide (4 g.) and the mixture boiled for ½ hr. After 48 hr. at room temperature the benzene was removed, and the residue dissolved in ice-cold sodium hydroxide solution, acidified, and steam-distilled. The colourless 5-bromothioindoxyl (0·2 g., 16%) had the m. p. of the product recorded by Pummerer,[13] who cyclised his substance with chlorosulphonic acid.

(ii) (4-Bromo-2-carboxyphenylthio)acetic acid (10 g.) and acetic anhydride (150 ml.) were refluxed for ½ hr., and the anhydride then removed *in vacuo*. The resulting deep red liquid was hydrolysed by an excess of refluxing alcoholic sodium hydroxide for ½ hr., and 5-bromothioindoxyl, m. p. 116°, was precipitated (90% yield) on acidification.

(iii) 33% Sodium hydroxide solution (3 ml.) was added to (4-bromo-2-cyanophenylthio)-acetic acid (2 g.) in water (40 ml.), and warmed to 80° for 15 min. Sodium chloride (12 g.) was added, and the precipitated sodium salt collected, washed with brine, and then added to 5% hydrochloric acid (30 ml.), heated at 95° for 15 min., filtered, and cooled. 5-Bromothioindoxyl, m. p. 114—115°, separated (1·1 g., 65%).

As in the conversion of (*o*-cyanophenylthio)acetic acid into thionaphthen-2-carboxylic acid (p. 2627), (4-bromo-2-cyanophenylthio)acetic acid (1 g.) gave *5-bromothionaphthen-2-carboxylic acid* (0·45 g., 48%), needles (from aqueous alcohol), m. p. 235° (Found : C, 42·4; H, 2·15. $C_9H_5O_2SBr$ requires C, 42·0; H, 1·95%).

5-Bromothionaphthen (VIII; R = 5-Br).—(i) Reduction of freshly prepared 5-bromothioindoxyl (0·4 g.) was effected by 1 hour's refluxing with amalgamated " mossy zinc " [from zinc dust (3 g.), activated for a short time with hydrochloric acid, washed, then treated with aqueous mercuric chloride] and glacial acetic acid (15 ml.). The cooled solution was made strongly alkaline and the product (0·3 g., 90%) isolated by steam-distillation and crystallisation from alcohol. 5-Bromothionaphthen formed colourless plates, m. p. 47° (Rabindran, Sunthankar, and Tilak [21] give m. p. 47°) (Found : Br, 37·8. Calc. for C_8H_5BrS : Br, 37·6%).

[21] Rabindran, Sunthankar, and Tilak, *Proc. Indian Acad. Sci.*, 1952, **36**, *A*, 405.

(ii) 5-Bromothionaphthen-2-carboxylic acid (0·25 g.), quinoline (5 ml.), and copper bronze (0·05 g.) were refluxed for 1½ hr. An ether extract of the acidified solution gave 5-bromothionaphthen, m. p. 47°, in 50% yield.

Thionaphthen-5-carboxylic acid (VIII; R = 5-CO_2H), made (0·48 g., 55%) from 5-bromothionaphthen (1 g.), as in the conversion [1] of 3-bromothionaphthen into thionaphthen-3-carboxylic acid, crystallised from aqueous alcohol, or much water, in needles, m. p. 211—212° (Found: equiv., 176. $C_9H_6O_2S$ requires equiv., 178).

(m-*Bromophenylthio*)*acetic Acid* (XVII).—(i) *m*-Bromobenzenesulphonyl chloride (50 g.) was refluxed with granulated zinc (125 g.) and concentrated hydrochloric acid (250 ml.) for 2 hr., then the *m*-bromothiophenol immediately steam-distilled into an agitated solution of chloroacetic acid (20 g.) containing excess of sodium hydroxide which was next heated on the water-bath for 45 min. Acidification of the filtered solution gave (m-*bromophenylthio*)*acetic acid*, granules (from water), m. p. 87° (overall yield, 60%) (Found: equiv., 247. $C_8H_7O_2BrS$ requires equiv., 247).

(ii) Though the interaction of diazotised anthranilic acid and aqueous sodium disulphide [25] has always smoothly produced dithiosalicylic acid in some 200 repetitions of the experiment made in this Department, nevertheless explosions occurred when diazotised *m*-bromoaniline or diazotised methyl anthranilate was used. However, diazotised *m*-bromoaniline was, by the use of potassium ethyl xanthate,[29] safely converted into *m*-bromothiocresol, which with chloroacetic acid and excess of sodium hydroxide gave (*m*-bromophenylthio)acetic acid in 60% overall yield. This was also obtained, in poor yield, by the addition of diazotised *m*-bromoaniline to mercaptoacetic acid.

4-*Bromo*-2-*nitroaniline*.—The nitration of *p*-bromoacetanilide with a mixture of nitric and sulphuric acid gives [15] 2 : 4-dibromo-6-nitroacetanilide and it is now found that this can be a product of Hübner's process [14] in which nitric acid (*d* 1·52) alone is used. However, *o*-nitroaniline is smoothly brominated [16] to 4-bromo-2-nitroaniline, easily convertible into 4-bromo-2-nitrobenzonitrile,[30] m. p. 97°.

(5-*Bromo*-2-*cyanophenylthio*)*acetic Acid* (XIX).—A solution of 4-bromo-2-nitrobenzonitrile (10 g.) and mercaptoacetic acid (15 ml.) in 1 : 1 aqueous alcohol (400 ml.) was made just alkaline to phenolphthalein with sodium hydroxide solution, and sodium acetate crystals (20 g.) were added. After 12 hours' refluxing most of the solvent was distilled off; the precipitate isolated after cooling crystallised from boiling water and then from alcohol, giving (5-*bromo*-2-*cyanophenylthio*)*acetic acid* (6·8 g., 60%), yellow needles, m. p. 196° (Found: S, 11·6. $C_9H_6O_2NBrS$ requires S, 11·75%).

6-*Bromothioindoxyl* (XVIII).—(i) (*m*-Bromophenylthio)acetic acid (25 g.) was boiled, until interaction ceased, with excess of thionyl chloride, of which the excess was removed *in vacuo*. To the resulting unisolated acid chloride in *o*-dichlorobenzene (200 ml.) powdered aluminium chloride (16 g.) was gradually added and the temperature was finally raised to 45°, the whole reaction requiring 40 min. Ice and sodium hydroxide were added until the mixture was alkaline, and the aqueous layer after extraction with ether was acidified, to give colourless 6-*bromothioindoxyl* (14 g., 60%), m. p. 153° (from alcohol), which rapidly became pink in air (Found: Br, 35·0. C_8H_5OBrS requires Br, 34·9%).

(ii) The same product was obtained in 60% yield from (5-bromo-2-cyanophenylthio)acetic acid by treatment with alkali and then acid as described for the preparation of 5-bromothioindoxyl from (4-bromo-2-cyanophenylthio)acetic acid.

6-*Bromothionaphthen* (VIII; R = 6-Br).—Reduction of bromothioindoxyls with zinc dust and concentrated hydrochloric or acetic acid or sodium hydroxide produces poor yields of the bromothionaphthens. In one instance 6-bromothioindoxyl was refluxed with zinc dust and glacial acetic acid for 3 hr. The steam-distillate, from the reaction mixture made alkaline, yielded to ether an oil of which the more volatile fraction (b. p. 105—110°/20 mm.) contained sulphur compounds. The higher fraction contained about a 15% yield of 6-bromothionaphthen. A better yield was obtained as follows. 6-Bromothioindoxyl (6 g.) was refluxed with glacial acetic acid (50 ml.) and amalgamated "mossy" zinc (from zinc dust, 12 g.) for 50 min. with stirring and the mixture made alkaline with sodium hydroxide and steam-distilled. The distillate gave a moderate yield of 6-*bromothionaphthen*, b. p. 139—140°/30 mm., which after vacuum sublimation formed prisms, m. p. 56° (Found: S, 15·1. C_8H_5BrS requires S, 15·0%).

[29] Cf. Tarbell and Fukushima, *Org. Synth.*, 1947, **27**, 81.
[30] Claus and Scheulen, *J. prakt. Chem.*, 1891, **43**, 203.

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Thionaphthen-6-carboxylic Acid.—Carboxylation of the Grignard complex, prepared from 6-bromothionaphthen as described for 5-bromothionaphthen, gave thionaphthen-6-carboxylic acid (50%) as needles, m. p. 162°, from alcohol (Found: equiv., 179·9. $C_9H_6O_2S$ requires equiv., 178).

(*o-Carboxyphenylthio*)*acetic Acid.*—This acid was prepared in 40% yield from anthranilic acid *via* dithiosalicylic acid [31] as described (p. 2627) for (4-bromo-2-carboxyphenylthio)acetic acid. The same acid has been obtained as follows. A diazotised solution, at <5°, of anthranilic acid [from anthranilic acid (7·5 g.), concentrated hydrochloric acid (10·7 ml.), and sodium nitrite (4·1 g.)] was added to mercaptoacetic acid (5 g.) in cold water (75 ml.) containing excess of sodium hydrogen carbonate, further quantities of the last being added as required to keep the solution neutral. Acidification gave the required (*o*-carboxyphenylthio)acetic acid, m. p. 214° (lit.,[32] m. p. 216—217°) in 34% yield.

Thioindoxyl-7-carboxylic Acid.—(i) (*o*-Carboxyphenylthio)acetic acid (65 g.) was converted into the acid chloride with thionyl chloride and cyclised in *o*-dichlorobenzene as for the preparation of 6-bromothioindoxyl. Thioindoxyl-7-carboxylic acid (90%) crystallised from water or aqueous alcohol in needles, m. p. 310° (Found: equiv., 193·8. $C_9H_6O_3S$ requires equiv., 194).

(ii) The acid chloride (from 0·5 g. of acid) in ether was treated with boron trifluoride (9·5 g.) in ether. After 3 days the solution was refluxed for 15 min., cooled, and extracted with dilute sodium hydroxide. Acidification of the alkaline extract gave thioindoxyl-7-carboxylic acid in 75% yield.

Thionaphthen-7-carboxylic Acid.—After reduction of thioindoxyl-7-carboxylic acid with amalgamated "mossy" zinc in boiling glacial acetic acid for ½ hr. the acetic acid was removed by steam, and thionaphthen-7-carboxylic acid crystallised from water, and then from aqueous alcohol, in needles, m. p. 172° (55%) (Found: equiv., 179. $C_9H_6O_2S$ requires equiv., 178).

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University of Melbourne, Australia. [*Received, December* 31*st*, 1956.]

[31] D.R.P. 181,658.
[32] Friedländer, *Annalen*, 1907, **351**, 403.

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510. *Researches on Ammines. Part XII.* Sulphatoaquotetramminocobaltic and Sulphatobisethylenediaminecobaltic Salts.*

By H. J. S. King and S. N. Mistry.

A general method for the preparation of sulphatobisethylenediaminecobaltic salts is given and the presence of the sulphato-ring in the complex is established. Solutions of sulphato-salts undergo more extensive aquation to diaquosulphates than do sulphatoaquo-salts. The method of distinguishing between ionised sulphate and the sulphato-complex is discussed.

It appeared remarkable that both the sulphito- and the sulphato-radicals occupy one position only in the sulphito- and sulphato-aquotetramminocobaltic complexes, and that no sulphito- or sulphato-tetrammines have been described. On the other hand, no sulphito- or sulphato-aquobisethylenediaminecobaltic salts are known, but sulphito- and sulphato-bisethylenediaminecobaltic salts, in which the sulphito- or sulphato-ring occupies two positions in the complex, have been described. In the present paper, the case of the sulphato-radical has been further investigated.

The sulphatoaquotetrammines were first described by Ephraim and Flugel [1] who based their formulation as aquo-salts on the presence of a water molecule which was not

* Part XI, *J.*, 1957, 2402.

[1] Ephraim and Flugel, *Helv. Chim. Acta*, 1924, **7**, 724.

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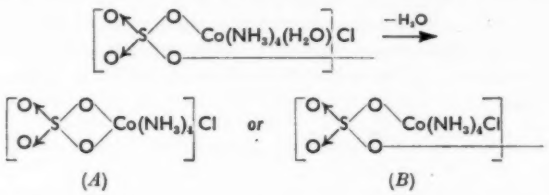
removed at 110°. Job [2] established the presence of the hydroxo–aquo-equilibrium by a conductometric titration with barium hydroxide, and this supported Ephraim and Flugel's formulation. It has now been shown that the sulphatoaquo-chloride $[Co(NH_3)_4(H_2O)(SO_4)]Cl$ yields, with moist silver oxide, a filtrate which is only slightly alkaline, indicating the presence of the non-valent complex $[Co(NH_3)_4(OH)(SO_4)]$. The pH of a 0·02M-solution was 8·56 at 23°, while the expected value for the sulphato-hydroxide $[Co(NH_3)_4(SO_4)]OH$ is about 12·3. This result further supports the formulation of the sulphatoaquotetrammines as aquo-salts. It was similarly shown in Part V [3] that the hydroxide obtained from $[Co(NH_3)_4(H_2O)_2]Cl_3$ is $[Co(NH_3)_4(OH)_2]OH$. Neither aquo- nor diaquo-hydroxides appear to exist.

By prolonged heating at 125°, the water molecule has been completely removed from the sulphatoaquo-chloride, yielding a product which may be the sulphatotetrammine containing the sulphato-ring (formula *A*), or a non-valent complex in which the sulphato-group still occupies one position only (formula *B*).* If (*A*) is correct, this is the only



(*A*) (*B*)

recorded salt of the sulphatotetramminocobaltic series. If the solid has structure (*B*), the complex must undergo immediate aquation with water, since the chlorine is immediately and completely precipitated by silver ion.

A cold solution of the sulphatoaquo-chloride gave a turbidity with barium chloride only after 10 min., whereas the cold solution of the dehydrated salt gave a turbidity forthwith. Thus partial aquation to $\left[Co(NH_3)_4(H_2O)_2\right]^{SO_4}_{Cl}$ takes place more rapidly in the latter case. A quantitative precipitation of the cold sulphatoaquo-chloride solution with barium chloride indicated that only 4% of the total sulphate radical was present as sulphate ions.

The only salt of the sulphatobisethylenediaminecobaltic series hitherto described is $[Co\ en_2(SO_4)]Br,H_2O$, obtained by Duff.[4] Though monohydrated, it became anhydrous on exposure to air, indicating a complex in which the sulphate radical is attached to cobalt by two links. This has been confirmed by preparation of the sulphate, chloride, and nitrate of the series, all of which were anhydrous. Quantitative investigation of the action of barium chloride indicated that in solution the equilibrium :

$$\left[Co\ en_2(SO_4)\right]X + 2H_2O \rightleftharpoons \left[Co\ en_2(H_2O)_2\right]^{SO_4}_{X}$$

lies further to the right than the equilibrium :

$$\left[Co(NH_3)_4(H_2O)(SO_4)\right]X + H_2O \rightleftharpoons \left[Co(NH_3)_4(H_2O)_2\right]^{SO_4}_{X}$$

Considerable difficulty was experienced in preparing the bisethylenediamine salts in pure condition, owing to their high solubility. Duff's method {treatment of $[Co\ en_2(CO_3)]Br$ with the calculated amount of sulphuric acid} proved unsatisfactory for salts other than the bromide. Attempts to prepare $[Co\ en_2(SO_4)]_2SO_4$ by treating $[Co\ en_2Cl_2]Cl$ with three

* We are indebted to a referee for this suggestion (*B*).

[2] Job, Thesis, Paris, 1921.
[3] King, *J.*, 1932, 1275.
[4] Duff, *J.*, 1922, 450.

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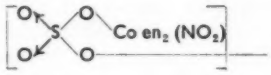
equivalents of silver sulphate were unsuccessful, as the chlorine was not completely eliminated as silver chloride. The method which gave the best results was based on one described in Part VII [5] for introducing bivalent acid radicals into the tetramminocobaltic and tetramminoaquocobaltic complexes. *trans*-Dichlorobisethylenediaminecobaltic chloride was converted into the *cis*-dihydroxo-hydroxide $[Co\ en_2(OH)_2]OH$ and the solution of this was treated with two equivalents of sulphuric acid and one equivalent of sulphuric, hydrochloric, or nitric acid.

Unsuccessful attempts to isolate solid dihydroxotetramminocobaltic salts were recorded in Part V.[3] When however *cis*-$[Co\ en_2(OH)_2]OH$ was treated with one equivalent of hydrochloric acid, the *cis*-dihydroxo-chloride $[Co\ en_2(OH)_2]Cl$ was isolated as a red amorphous solid.

It has been shown in Part XI [6] that sulphatoaquotetramminocobaltic nitrite isomerises to nitroaquotetramminocobaltic sulphate. When sulphatobisethylenediaminecobaltic chloride was treated with one equivalent of silver nitrite, the filtrate yielded a brown amorphous solid which contained no water and from the method of preparation might be expected to be sulphatobisethylenediaminecobaltic nitrite $[Co\ en_2(SO_4)]O{\cdot}NO$. However, it gave no oxides of nitrogen even when heated with concentrated hydrochloric acid, and this supports the alternative formulation * as the non-valent complex, nitrosulphatobisethylenediaminecobalt :



If this formula is correct, this is the only recorded sulphatobisethylenediaminecobaltic complex in which the sulphato-group is attached to cobalt by one link only. Quantitative precipitation with barium chloride indicated that only 64% of the sulphate radical remained un-ionised in the aqueous solution, so the equilibrium :

$$[Co\ en_2(SO_4)(NO_2)] + H_2O \rightleftharpoons [Co\ en_2(H_2O)(NO_2)]SO_4$$

was probably established.

It is usual to ascertain whether a chloride or sulphate radical is present in the ionised condition or as part of a complex ion by precipitation tests with silver or barium salts respectively. If no immediate precipitate is obtained at room temperature, the acid radical is entirely in the complex. For a stable complex ion where no aquation occurs, this method gives a reliable indication. If however an equilibrium such as :

$$\left[Co\ en_2(SO_4)\right]X + 2H_2O \rightleftharpoons \left[Co\ en_2(H_2O)_2\right]^{SO_4}_{X}$$

is established in the solution, addition of barium ion will displace the equilibrium to the right, and a larger proportion of ionised sulphate may be indicated than is actually present in the pure aqueous solution, even if the barium sulphate is collected immediately. Hence the value obtained for the proportion of ionised sulphate may be expected to be somewhat higher than the correct value. This must be borne in mind in interpreting the data in the Table on p. 2634. Job and Urbain [7] suggested that barium chloride is not a suitable reagent for distinguishing ionised from un-ionised sulphate, and recommended benzidine hydrochloride instead. We find that benzidine hydrochloride has no advantages over barium chloride, if precipitation of ionised sulphate in the latter case is carried out in the cold, and the barium chloride is immediately separated by centrifuging.

* We are indebted to a referee for this suggestion also.

[5] King, *J.*, 1933, 517.
[6] King and Mistry, *J.*, 1957, 2402.
[7] Job and Urbain, *Compt. rend.*, 1920, **170**, 843.

Experimental

Sulphatoaquotetramminocobaltic chloride was prepared from the sulphate as described by Ephraim and Flugel [1] {Found : Co, 21·3; NH_3, 24·7; SO_4, 34·8; Cl, 12·8; H_2O, 6·5. Calc. for $[Co(NH_3)_4(H_2O)(SO_4)]Cl$: Co, 21·3; NH_3, 24·6; SO_4, 34·7; Cl, 12·8; H_2O, 6·5%}. Water was completely removed, without loss of ammonia, in 96 hr. at 125°. The pink sulphatoaquochloride was very soluble to a deep-red acid solution. Barium chloride gave a turbidity only after 10 min. and a quantitative precipitation indicated that in the cold freshly prepared solution 96% of the sulphate radical was un-ionised. The dehydrated salt was less soluble, and the pale-pink acid solution gave a slight turbidity with barium chloride forthwith, and a further precipitate on standing or heating. Chlorine in the dehydrated salt was immediately and completely precipitated by silver ion.

Sulphatohydroxotetramminocobalt $[Co(NH_3)_4(OH)(SO_4)]$ was obtained in solution as a deep-red filtrate, only slightly alkaline to litmus, when sulphatoaquotetramminocobaltic chloride was triturated for 5 min. with freshly prepared moist silver oxide from four parts of silver nitrate. Attempts to isolate the solid product were unsuccessful. The pH of a freshly prepared 0·02M-solution at 23° was found to be 8·56, by using a standardised pH meter with glass electrode and calomel reference electrode.

trans-Dichlorobisethylenediaminecobaltic chloride was prepared by the method given in *Inorg. Synth.*[2] $[Co\ en_2Cl_2]Cl,HCl$ was converted into $[Co\ en_2Cl_2]Cl$ at 95° in 4 hr., as decomposition sometimes occurred at the recommended temperature of 110° (Found : Co, 20·7; N, 19·4; Cl, 37·4. Calc. for $[Co\ en_2Cl_2]Cl$: Co, 20·7; N, 19·6; Cl, 37·3%).

Sulphatobisethylenediaminecobaltic Sulphate.—*trans*-$[Co\ en_2Cl_2]Cl$ (2 g.) was triturated with freshly prepared moist silver oxide (from 8 g. of silver nitrate), for 5 min. Silver chloride and excess of silver oxide were filtered off and washed with the minimum amount of water, till the filtrate was colourless. The deep-red filtrate (30 ml.), containing *cis*-$[Co\ en_2(OH)_2]OH$, was mixed with N-sulphuric acid (21·0 ml., 3 equivs.). The pale-red solution was heated to the b. p., and became dark-red. It was taken to dryness in a vacuum over sulphuric acid, yielding the dark-red amorphous *sulphato-sulphate*, very soluble and very hygroscopic {Found : Co, 18·2; N, 17·3; SO_4, 44·6. $[Co\ en_2(SO_4)]_2SO_4$ requires Co, 18·2; N, 17·3; SO_4, 44·6%}.

Sulphatobisethylenediaminecobaltic Nitrate.—*trans*-$[Co\ en_2Cl_2]Cl$ (2 g.) was converted into *cis*-$[Co\ en_2(OH)_2]OH$ solution (30 ml.) and this was treated successively with one equiv. of 0·5N-nitric acid and two equivs. of N-sulphuric acid. After concentration by boiling, the solution was taken to dryness in a vacuum over sulphuric acid, yielding the red, very hygroscopic and very soluble amorphous *sulphato-nitrate* (1·7 g.). The cold solution gave a turbidity with barium chloride only after several minutes {Found : Co, 17·3; N, 20·7; SO_4, 28·2. $[Co\ en_2(SO_4)]NO_3$ requires Co, 17·5; N, 20·8; SO_4, 28·5%}.

Sulphatobisethylenediaminecobaltic chloride was prepared similarly, with one equiv. of hydrochloric acid and two of sulphuric acid. The red amorphous product (1·9 g.) was hygroscopic and very soluble, and the solution gave a turbidity with barium chloride only after a few minutes {Found : Co, 18·9; Cl, 11·3; SO_4, 30·8. $[Co\ en_2(SO_4)]Cl$ requires Co, 18·9; Cl, 11·4; SO_4, 30·9%}.

Sulphatobisethylenediaminecobaltic bromide was obtained in monohydrated form by Duff,[4] by treating $[Co\ en_2(CO_3)]Br$ with two equivs. of sulphuric acid. It has also been obtained as above by treating $[Co\ en_2(OH)_2]OH$ from $[Co\ en_2Cl_2]Cl$ (2 g.) with hydrobromic acid (1 equiv.) and sulphuric acid (2 equivs.) (yield 2·3 g.) {Found : Co, 16·6; Br, 22·5; SO_4, 27·1. Calc. for $[Co\ en_2(SO_4)]Br$: Co, 16·6; Br, 22·5; SO_4, 27·1%}.

Nitrosulphatobisethylenediaminecobalt.—The salt $[Co\ en_2(SO_4)]Cl$ (2 g.) was shaken for 3 hr. at 0° with silver nitrite (0·991 g.) and water (20 ml.). Silver chloride was separated and washed with the minimum amount of ice-cold water. The filtrate was taken to dryness in a vacuum over sulphuric acid, and yielded dark-brown amorphous *nitrosulphatobisethylenediaminecobalt* (1 g.), very soluble, and giving in solution only a slight turbidity with barium chloride in the cold, increasing considerably on boiling {Found : Co, 18·3; N, 21·8; SO_4, 29·9. $[Co\ en_2(SO_4)(NO_2)]$ requires Co, 18·3; N, 21·8; SO_4, 29·9%}. No oxides of nitrogen were evolved with dilute or concentrated hydrochloric acid, even on boiling.

cis-*Dihydroxobisethylenediaminecobaltic Chloride.*—*trans*-$[Co\ en_2Cl_2]Cl$ (2 g.) was converted into *cis*-$[Co\ en_2(OH)_2]OH$ in water (30 ml.), and one equiv. of 0·1N-hydrochloric acid was added.

[2] *Inorg. Synth.*, 1946, **2**, 223.

The pale-red solution, when concentrated by boiling, became deep-red, and was taken to dryness in a vacuum over sulphuric acid, yielding the red amorphous *dihydroxo-chloride* (0·8 g.), hygroscopic, and very soluble to a strongly alkaline dark-red solution {Found : Co, 23·7; Cl, 14·1. $[Co\ en_2(OH)_2]Cl$ requires Co, 23·7; Cl, 14·2%}.

Determination of Ionised and Un-ionised Sulphate Radical in Sulphato- and Sulphatoaquo-salts.—The salt (0·5 g.) in water (30 ml.) was treated in the cold with the calculated amount of barium chloride in water (15 ml.), then immediately centrifuged for 2 min. The barium sulphate was collected and weighed, giving the weight of ionised sulphate. The solution and washings were kept for 24 hr. and finally boiled with excess of barium chloride. From the further weight of barium sulphate thus obtained, the weight of un-ionised sulphate radical was calculated. A similar method was used when benzidine hydrochloride was the precipitant. The results are tabulated.

Salt	Precipitant	Un-ionised sulphate (%)	Ionised sulphate (%)
$[Co(NH_3)_4(H_2O)(SO_4)]Cl$	$BaCl_2$	95·8	4·2
$[Co(NH_3)_4(H_2O)(SO_4)]_2SO_4$	$BaCl_2$	39·0	61·0
,,	$C_{12}H_8(NH_2)_2,2HCl$	38·4	61·6
$[Co\ en_2(SO_4)]Cl$	$C_{12}H_8(NH_2)_2,2HCl$	50·7	49·3
$[Co\ en_2(SO_4)]Br$	$BaCl_2$	64·4	35·6
$[Co\ en_2(SO_4)]NO_3$	$BaCl_2$	73·7	26·3
$[Co\ en_2(SO_4)]_2SO_4$	$BaCl_2$	44·4	55·6
,,	$C_{12}H_8(NH_2)_2,2HCl$	44·9	55·1
$[Co\ en_2(SO_4)(NO_2)]$	$BaCl_2$	64·1	35·9

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511. 7-*Nitro*-1-*naphthylamine. Part II.*[1] *The Nitration of* N-*Acyl Derivatives and Decompositions of Diazotised* 2 : 4 : x-*Trinitro*-1-*naphthylamines.*

By A. HARDY and E. R. WARD.

Nitration of three *N*-acyl-7-nitro-1-naphthylamines has been studied, the predominant mononitration of the toluene-*p*-sulphonyl derivative in the 2-position being noteworthy. Decompositions of diazotised 2 : 4 : 7-trinitro-1-naphthylamine, compared with those of other diazotised 2 : 4 : *x*-trinitro-1-naphthylamines, indicate the decisive influence of internuclear effects on their reactivity. 1 : 4 : 6-Trinitronaphthalene has been prepared and is further nitrated to 1 : 3 : 5 : 8-tetranitronaphthalene only.

IN halogenation or diazo-coupling of 7-nitro-1-naphthylamine or its *N*-acetyl derivative monosubstitution was restricted to the 4-position, and further substitution, when it occurred, was at the 2-position. Nitration of *N*-acyl derivatives is much more complex. Whereas the *N*-acetyl derivative is mononitrated at both the 2- and the 4-position, with the latter clearly the more activated, the *N*-toluene-*p*-sulphonyl derivative reacts predominantly at the 2-position.

In previous studies of the nitration, in acetic acid above room temperature, of *N*-toluene-*p*-sulphonyl derivatives from 5-, 6-, and 8-nitro-1-naphthylamines [2,3] only simultaneous dinitration at the 2- and the 4-position was recorded. With 7-nitro-1-naphthylamine we find that the products depend on whether the reaction is conducted in solution or suspension, on the temperature, and on the amount of nitrating acid. Our extended studies were only made possible by chromatography. Thus, in suspension at 20—30°, with more than sufficient nitric acid to cause dinitration, 2 : 7-dinitro- and 2 : 4 : 7-trinitro-1-naphthylamine were obtained (after hydrolysis) the latter predominating. At 85° the trinitro-amine, with a trace of 2 : 7-dinitro-1-naphthylamine, was obtained. In

[1] Part I, Hardy, Ward, and Day, *J.*, 1956, 1979.
[2] Hodgson and Turner, *J.*, 1942, 723; 1943, 791.
[3] Ward and Day, *J.*, 1951, 782.

neither case was 4 : 7-dinitro-1-naphthylamine detected, even by chromatography. But by nitration in solution at 20° with only enough acid to effect mononitration, a mixture of 2 : 7- and 4 : 7-dinitro-1-naphthylamine was obtained, the former predominating. It appears therefore that the 2-position is the more activated, but it is difficult to see why some 4 : 7-dinitro-1-naphthylamine is not *always* found with the 2 : 7-isomer.

Investigation of the nitration of 7-nitro-*N*-phthaloyl-1-naphthylamine was limited by difficulty in hydrolysing the product, the yield of hydrolysed amines being equivalent to only about a third of the starting material; the identity of the polynitronaphthylamines isolated suggests that some nitration products may have been destroyed. Thus 2 : 7- and 4 : 7-dinitro-1-naphthylamine were obtained (demonstrating mononitration at both the 2- and the 4-position) but no 2 : 4 : 7-trinitro-1-naphthylamine although a new trinitro-1-naphthylamine was formed. The relative proportion of isomers isolated in these circumstances can be of little significance. Electrophilic substitution at positions other than 2 or 4 has never been observed with the related 5-, 6-, or 8-nitro-1-naphthylamine (although the nitration of their *N*-phthaloyl derivatives has not been studied).

4 : 7-Dinitro-1-naphthylamine was oriented by diazotisation and deamination to 1 : 6-dinitronaphthalene but deamination of 2 : 7-dinitro-1-naphthylamine by Hodgson and Turner's [4] or Hodgson and Birtwell's method [5] gave unidentifiable products. The 2 : 7-dinitro-amine was oriented by the fact that its diazonium salt readily gave a diazo-oxide, also by conversion of the diazonium compound into 1-bromo-2 : 7-dinitronaphthalene, followed by dehalogenation of this to 2 : 7-dinitronaphthalene by Smith's method.[6] A similar dehalogenation carried out on the corresponding 1-chloro-2 : 7-dinitronaphthalene gave only unchanged starting material. 2 : 4 : 7-Trinitro-1-naphthylamine was oriented by reason of the fact that after diazotisation it readily gave a diazo-oxide (confirming 2-nitration) and could not be further brominated (showing that the 4-position was already occupied), whilst 2 : 7- and 4 : 7-dinitro-1-naphthylamine were readily monobrominated under analogous conditions.

The new trinitro-1-naphthylamine is unlikely to contain adjacent nitro-groups in one nucleus. Since the diazotised amine does not give a diazo-oxide there cannot be a nitro-group at position 2 (or at 3 : 4 since 3 : 4-dinitro-1-naphthylamine very readily gives a 1 : 4-diazo-oxide [7]), and the most likely structure appears to be 4 : 5 : 7-trinitro-1-naphthylamine.

Attempts to deaminate diazotised 2 : 4 : 7-trinitro-1-naphthylamine by the methods cited above [4, 5] failed. The only product from the Sandmeyer reaction that could be identified by chromatography was 1-diazo-4 : 7-dinitro-2-naphthol, although small amounts of products containing appreciable amounts of halogen were also isolated (almost certainly arising by Sandmeyer decompositions of the diazo-oxide). The results are analogous to those obtained, in similar circumstances,[3, 7] with other 2 : 4 : *x*-trinitro-1-naphthylamines (*x* = 3, 5, 6, or 8). We conclude that with all these diazotised trinitronaphthylamines the tendency to form a diazo-oxide, even in the concentrated acid medium of a Sandmeyer decomposition, is so strong that normal reaction either does not occur at all or does so only to a minor extent. This behaviour can be contrasted with that of diazotised 2 : 4-dinitro-1-naphthylamine, which under analogous conditions gives excellent yields of 1 : 3-dinitronaphthalene by deamination [8] and of 1-chloro-2 : 4-dinitronaphthalene by Sandmeyer decomposition.[9] The introduction of a 3-, 5-, 6-, 7-, or 8-nitro-group into 2 : 4-dinitro-1-naphthylamine might perhaps be expected to exert little effect on the reactivity of the diazonium salt since at the 3-position it is *meta* to the diazo-group and in the other

[4] Hodgson and Turner, *J.*, 1942, 748.
[5] Hodgson and Birtwell, *J.*, 1944, 112.
[6] Smith, *J. Amer. Chem. Soc.*, 1949, **71**, 2885.
[7] Ward, Pierce, and Wells, unpublished work; Ward, Thesis, London, 1946; Coulson, Thesis, London, 1955; Staedel, *Ber.*, 1881, **14**, 898; *Annalen*, 1883, **217**, 153, 173, 174; Hodgson and Hathway, *J.*, 1944, 651.
[8] Hodgson and Birtwell, *J.*, 1943, 433.
[9] Hodgson and Ward, *J.*, 1948, 2017.

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compounds it is not in the same nucleus as the diazo-group. In any case it should increase the positivity of the 1-carbon atom and facilitate diazo-decompositions. It is clear however that the introduction of this third nitro-group exerts a decisive effect on the reactivity of the diazonium salts and it appears that the positivity of the 1-carbon atom is increased sufficiently to render it more prone to nucleophilic attack by water molecules (despite the acidic medium), forming a diazo-oxide rather than undergoing the alternative " normal " diazo-decomposition. The effect of the third nitro-group might well be interpreted as an overall effect on the molecule (somewhat analogous to the displacement of a nitro-group from 1 : 3 : 5-trinitrobenzene by nucleophilic reagents), complications due to steric factors in 2 : 3 : 4- or 2 : 4 : 8-trinitro-1-naphthylamine and the quinonoid or non-quinonoid disposition of the third nitro-group to the (1-)diazo-group being borne in mind. Whatever may be the explanation internuclear effects arising from the substitution of a further nitro-group at position 5, 6, 7, or 8 are of definite significance and this is probably one of the best available demonstrations of electronic interaction between groups in different nuclei in a naphthalene molecule, such interactions usually being regarded as weak when compared to effects transmitted within one nucleus (cf. Bunnett and Zahler [10]). Interaction of polynitronaphthalenes with aqueous-methanolic sodium hydrogen sulphide,[11] which can lead to nucleophilic displacement of nitro-groups, also indicated internuclear activation whereas such effects were not apparent in reactions between polynitronaphthalenes and sodium nitrophenyl sulphides,[12] displacement of nitro-groups in the latter reaction requiring at least two nitro-groups in any nucleus to be in 1 : 2-, 2 : 3-, or 1 : 4-positions.

By a Sandmeyer reaction from diazotised 2 : 4 : 5-trinitro-1-naphthylamine Ward and Day [3] obtained a substance designated as crude 1-chloro-2 : 4 : 5-trinitronaphthalene and dehalogenated it in an attempt to prepare 1 : 3 : 5-trinitronaphthalene but the product differed from that described by Dimroth and Ruck.[13] This result is not surprising if considered in terms of the diazo-decompositions discussed above and the Sandmeyer product was probably largely material arising from the diazo-oxide rather than the expected trinitrochloro-compound. Authentic 1 : 3 : 5-trinitronaphthalene has now been prepared by diazo-decomposition from 3 : 5-dinitro-1-naphthylamine and its identity with Dimroth and Ruck's compound established by infrared spectra.

The new 1 : 4 : 6-trinitronaphthalene was obtained from diazotised 4 : 7-dinitro-1-naphthylamine by the method of Hodgson, Mahadevan and Ward,[14] but a similar decomposition of diazotised 2 : 7-dinitro-1-naphthylamine failed to yield 1 : 2 : 7-trinitronaphthalene. In other investigations [15] we failed to obtain 1 : 2 : 4-trinitronaphthalene from 2 : 4- or 3 : 4-dinitro-1-naphthylamine, 1 : 2 : 5-trinitronaphthalene from 2 : 5-dinitro-1-naphthylamine, or 1 : 2 : 8-trinitronaphthalene from 1 : 8-dinitro-2-naphthylamine : in each case diazo-oxide formation in the aqueous decomposition medium intervenes to prevent replacement of the diazonium by the nitro-group.

1 : 4 : 6-Trinitronaphthalene is further nitrated in sulphuric acid to 1 : 3 : 5 : 8-tetranitronaphthalene only, as expected from the simplest considerations but also in agreement with calculations by the theoretical treatment of Sixma,[16] as applied to nitrations of other polynitronaphthalenes.

Experimental

Ultraviolet Absorption Spectrum of 7-Nitro-1-naphthylamine.—The spectrum was recorded by means of a Unicam SP 500 photoelectric spectrophotometer, the concentration of amine being 0·010 g. of amine per l. of absolute ethanol or *cyclo*hexane. Maxima and, in parentheses,

[10] Bunnett and Zahler, *Chem. Rev.*, 1951, **49**, 273.
[11] Hodgson and Ward, *J.*, 1949, 1187; Ward, Coulson, and Hawkins, *J.*, 1954, 2974.
[12] Hodgson and Ward, *J.*, 1948, 2017; cf. Coulson, ref. 7.
[13] Dimroth and Ruck, *Annalen*, 1926, **446**, 123.
[14] Hodgson, Mahadevan, and Ward, *J.*, 1947, 1392.
[15] Ward, Hawkins, Pierce, and Wells, unpublished work.
[16] Sixma, *Rec. Trav. chim.*, 1954, **73**, 235.

log E, were: in EtOH, 2240 (4·47), 2860 (4·28), 3400 sh (3·42), 4380 (3·62): in *cyclo*hexane, 2210 (4·52), 2780 (4·38), 3080 (3·51), 3320 sh (3·34), 4020 (3·64).

7-*Nitro*-N-*toluene*-p-*sulphonyl*-1-*naphthylamine*.—A mixture of the amine (10 g.) and toluene-*p*-sulphonyl chloride (15 g.) was added slowly, with stirring, to pyridine (30 c.c.). After being heated on the water-bath for 30 min. the mixture was poured into 10% w/v hydrochloric acid (500 c.c.), and the solids were collected, washed with water, and dissolved in warm 2% aqueous sodium hydroxide (500 c.c.). The extract was filtered and acidified by hydrochloric acid, and the solids (17·5 g., 95%) were washed with water; the *product*, crystallised from methanol, had m. p. 208—209° (Found: N, 7·9; S, 9·2. $C_{17}H_{14}O_4N_2S$ requires N, 8·2; S, 9·4%).

7-*Nitro*-N-*phthaloyl*-1-*naphthylamine*.—The amine (5 g.) and phthalic anhydride (5 g.) were fused together for 5 min. and after cooling extracted with boiling acetic acid (150 c.c.). The extract was refluxed with charcoal, filtered hot, and by concentration to small volume gave 7-nitro-*N*-phthaloyl-1-naphthylamine (6·8 g., 90%), m. p. 252° (from acetic acid) (Found: C, 66·2; H, 3·3. Calc. for $C_{18}H_{10}O_4N_2$: C, 67·9; H, 3·2%).

Nitration of N-*Acetyl*-7-*nitro*-1-*naphthylamine*.—The acetyl compound (10 g.) was stirred into nitric acid (*d* 1·5; 10 c.c.) during 40 min. at 12—15°, then set aside for 1 hr., poured on ice and the yellow precipitate of mixed *N*-acetyl-2 : 7- and -4 : 7-dinitro-1-naphthylamine collected (10·8 g., 90%). The mixed amides (5 g.) were refluxed with 0·025N-sodium methoxide in methanol (250 c.c.) for 90 min. and filtered hot, affording 4 : 7-dinitro-1-naphthylamine, which when washed with methanol had m. p. 283° (2·0 g., 47% calc. on amides). The filtrate was poured on ice, yielding impure 2 : 7-dinitro-1-naphthylamine, m. p. 200—214° (2·0 g., 47%) (combined yield on hydrolysis, *ca.* 94%). Alternatively hydrolysis by refluxing ethanol and aqueous sulphuric acid (50% w/v) gives almost a quantitative yield of dinitronaphthylamines. From this mixture (A), 4 : 7-dinitro-1-naphthylamine (40%) is separated by refluxing with methanol (55 c.c./g.), the hot solution being filtered and poured on ice; this yields impure 2 : 7-dinitro-1-naphthylamine (43%).

The pure dinitronaphthylamines were prepared by chromatography of the products from the original hydrolysis in benzene on alumina, with (4 : 1, v/v) benzene–ethanol for elution. Each contained traces of the other, as shown by the formation of two bands on the columns. 2 : 7-*Dinitro*-1-*naphthylamine* was obtained as yellow needles, m. p. 252° (Found: N, 18·1. $C_{10}H_7O_4N_3$ requires N, 18·1%), and 4 : 7-*dinitro*-1-*naphthylamine* as red needles, m. p. 288° (Found: C, 51·3; H, 3·15. $C_{10}H_7O_4N_3$ requires C, 51·5; H, 3·03%).

Spectrographic analysis of the mixture (A) (By J. G. Hawkins). The measurements were as described [17] earlier for a similar mixture. The spectra of pure 2 : 7- and 4 : 7-dinitro-1-naphthylamine were compared with that of the mixture (A) and, after allowance for differences in the thickness of the films, the amounts were judged to represent 35 ± 10% of 2 : 7-, and 65 ± 10% of 4 : 7-dinitro-1-naphthylamine. All absorption peaks in the mixture were accounted for and further comparison with known spectra failed to show the presence of 7-nitro-1-naphthylamine.

Diazotisation and Diazo-decompositions of 2 : 7- *and* 4 : 7-*Dinitro*-1-*naphthylamines*.—Both amines were readily diazotised by Hodgson and Turner's method.[18] The diazonium salt from 4 : 7-dinitro-1-naphthylamine was deaminated, giving 1 : 6-dinitronaphthalene (43%), but the salt from 2 : 7-dinitro-1-naphthylamine gave no identifiable products. However the latter when poured into water containing sodium acetate, afforded 1-*diazo*-7-*nitro*-2-*naphthol* (from dioxan; charcoal), m. p. 160—162° (decomp.) (Found: C, 55·6; H, 3·0. $C_{10}H_5O_3N_3$ requires C, 55·8; H, 2·3%). 1-*Chloro*-2 : 7-*dinitronaphthalene* (50%), m. p. 132—133° (Found: Cl, 13·8. $C_{10}H_5O_4N_2Cl$ requires Cl, 14·0%), 1-*bromo*-2 : 7-*dinitronaphthalene* (50%), m. p. 137—138° (Found: Br, 26·8. $C_{10}H_5O_4N_2Br$ requires Br, 26·9%), and 1-*bromo*-4 : 7-*dinitronaphthalene* (40%), m. p. 148° (Found: Br, 27·5%), were prepared by adding the diazonium solutions to solutions of the appropriate cuprous halide (1 g./g. of amine) in the concentrated halogen acid (10 c.c./g.), storage overnight, pouring on ice, extraction of the dried product with hot ethanol, and crystallisation of material from the extract from light petroleum (b. p. 100—120°).

Dehalogenation of 1-bromo-2 : 7-dinitronaphthalene by Smith's method [6] gave 2 : 7-dinitronaphthalene (40%) but the chloro-analogue yielded only unchanged starting material.

Nitration of 7-*Nitro*-N-*toluene*-p-*sulphonyl*-1-*naphthylamine*.—(a) *Nitration in suspension at* 20—30°. The amide (1 g.) in acetic acid (2 c.c.) was treated with 1 : 1 v/v nitric acid (*d* 1·5)–acetic acid (0·55 c.c.; 10% excess for dinitration) during 15 min. at 20—30°. After storage

[17] Ward, Coulson, and Hawkins, *J.*, 1954, 918.
[18] Hodgson and Turner, *J.*, 1943, 86.

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overnight the solids were collected, washed with ether, and dried (0·80 g., 63% calc. as trinitroamide). A portion (0·2 g.) was chromatographed in benzene on alumina; elution with benzene–ethanol (3 : 1) gave 3 bands which successively yielded a resin (0·005 g.), 2 : 7-*dinitro*-N-*toluene*-p-*sulphonyl*-1-*naphthylamine* (0·075 g.), m. p. 195—200° (Found: C, 52·2; H, 3·5; S, 7·5. $C_{17}H_{13}O_6N_3S$ requires C, 52·6; H, 3·4; S, 8·3%), and water-soluble orange-yellow needles (0·120 g.), m. p. 283° (decomp.), probably the aluminium derivative of 2 : 4 : 7-trinitro-1-naphthol (m. p. unchanged on crystallisation from aqueous ethanol) (Found: C, 42·5; H, 2·4; Al, 3·1. Calc. for $C_{36}H_{12}O_{21}N_9Al$: C, 41·7; H, 1·4; Al, 3·1%). The dinitroamide was identified by hydrolysis to the dinitro-amine.

The original nitration product (0·60 g.) was hydrolysed by sulphuric acid (*d* 1·84; 1 c.c.) at 40° for 5 min. (yield 0·34 g.). This product was chromatographed in benzene on alumina, elution being by benzene–ethyl acetate (4 : 1) and then benzene–ethanol (7 : 3). This yielded both pure 2 : 7-dinitro-1-naphthylamine and 2 : 4 : 7-trinitro-1-naphthylamine (recovery 85%), the latter predominating.

(b) *Nitration in suspension at* 85°. The amide (10·0 g.) in acetic acid (16 c.c.) with a crystal of sodium nitrite was nitrated at 65° by the addition during 20 min. of nitric acid (*d* 1·5; 2·7 c.c.) in acetic acid (2·7 c.c.). The mixture was then heated at 85° for 5 min. and cooled in ice for 30 min. and the solids were collected and washed with ether, yielding 2 : 4 : 7-*trinitro*-N-*toluene*-p-*sulphonyl*-1-*naphthylamine*, m. p. 199—200° (60—75%) (from aqueous acetic acid; charcoal) (Found: C, 47·6; H, 3·05; S, 7·8. $C_{17}H_{12}O_9N_4S$ requires C, 47·2; H, 2·8; S, 7·4%). Hydrolysis as above gave 2 : 4 : 7-*trinitro*-1-*naphthylamine*, m. p. 251—253° (from ethanol) (Found: C, 43·5; H, 2·45. $C_{10}H_6O_6N_4$ requires C, 43·1; H, 2·2%). Chromatography of the hydrolysed nitration product as above gave a tiny amount of 2 : 7-dinitro-1-naphthylamine in addition to the trinitronaphthylamine.

(c) *Nitration in solution at* 20°. The amide (2 g.) in acetic acid (100 c.c.) was treated with nitric acid (*d* 1·5; 0·25 c.c., 1·02 mol.) in acetic acid (10 c.c.), added dropwise during 10 min. at 20°. After 24 hr. the solution was evaporated in a vacuum to 5 c.c., and the solids were collected and washed with acetic acid. A further amount was obtained by pouring the original filtrate into ice-water (combined yield, 92% for mononitration). After hydrolysis the mixed dinitronaphthylamines (1·20 g., 88% overall yield) were extracted portionwise with hot 9 : 1 v/v benzene–ethyl acetate (800 c.c. in all). The extract was filtered to remove an insoluble brown residue (0·3 g.; m. p. >300°) and chromatographed on alumina, elution being with 4 : 1 v/v benzene–ethyl acetate, which gave two bands. The first, yellow band yielded pure 2 : 7-dinitro-1-naphthylamine (0·47 g., 35%) and the second, orange band yielded pure 4 : 7-dinitro-1-naphthylamine (0·25 g., 19%).

Attempts to prepare the *N*-toluene-*p*-sulphonyl derivatives of 2 : 7- and 4 : 7-dinitro-1-naphthylamine by the usual methods failed.

Nitration of 7-*Nitro*-N-*phthaloyl*-1-*naphthylamine*.—The phthalimide (2·3 g.) was added during 30 min. to nitric acid (*d* 1·5; 10 c.c.) below 5°, kept for a further hour at this temperature, then poured on ice, and the product (2·5 g., 98% for mononitration) collected (Found: C, 58·1; H, 3·3. Calc. for a dinitronaphthylphthalimide: C, 59·5; H, 2·5%).

The product (2·3 g.) was hydrolysed by aqueous ammonia (*d* 0·88; 5 c.c.) for 1 hr. at 120°. The black product was washed with water, dried (1·6 g.), then extracted portionwise with 9 : 1 v/v benzene–ethyl acetate (300 c.c. total), and the cooled extract chromatographed on alumina. Elution by the original solvent and then by 3 : 1 v/v benzene–ethyl acetate produced four bands on the column which yielded successively 2 : 7-dinitro-1-naphthylamine (0·050 g.; m. p. 248°), some tar, 4 : 7-dinitro-1-naphthylamine (0·215 g.; m. p. 288°), and a red 7 : x : x-*trinitro*-1-*naphthylamine* (0·225 g.), m. p. 265 (decomp.) (Found: C, 43·1; H, 2·5. $C_{10}H_6O_6N_4$ requires C, 43·2; H, 2·2%) (total yield calc. as dinitronaphthylamines, *ca.* 33%). Similar products, but in lower yield (*ca.* 18%), were obtained by refluxing the nitration product (2·5 g.) with ethanol (15 c.c.) and hydrazine hydrate (90—95% w/w; 1 c.c.) for 2 hr.

The trinitronaphthylamine was diazotised by Hodgson and Turner's method;[18] the diazonium solution coupled readily with alkaline β-naphthol, but did not give a diazo-oxide on addition to ice-water. Attempted deamination by Hodgson and Turner's method [4] yielded a tiny amount of material which was not 1 : 6 : 7-trinitronaphthalene (Coulson [7]) but may have been impure 1 : 3 : 8-trinitronaphthalene.

Diazotisation and Diazo-decompositions of 2 : 4 : 7-*Trinitro*-1-*naphthylamine*.—The amine

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was diazotised by Hodgson and Turner's method employing a solution in sulphuric acid obtained by hydrolysis of the *N*-toluene-*p*-sulphonyl derivative. Addition of the diazo-solution to water gave an almost quantitative yield of 1-*diazo*-4 : 7-*dinitro*-2-*naphthol*, m. p. 158° (decomp) (from dioxan) (Found : C, 46·8; H, 1·8. $C_{10}H_4O_5N_4$ requires C, 46·2; H, 1·5%). The diazo-oxide (1·0 g.) was refluxed with ethanol (30 c.c.) and freshly prepared copper powder (0·3 g.) till the liquid no longer coupled with alcoholic alkaline resorcinol (*ca.* 3 hr.). Charcoal (0·4 g.) was added and after another hour's refluxing the mixture was filtered hot and, on cooling, deposited 4 : 7-*dinitro*-2-*naphthol*; this was washed with water, dried (0·2 g., 22%), and crystallised from aqueous alcohol as greenish-yellow needles, m. p. 215—217° (Found : C, 51·3; H, 2·9. $C_{10}H_6O_5N_2$ requires C, 51·3; H, 2·6%); 4 : 7-*dinitro*-2-*naphthyl acetate* had m. p. 155—156° (Found : C, 52·0; H, 2·9. $C_{12}H_8O_6N_2$ requires C, 52·2; H, 2·9%).

Attempts to produce 1 : 3 : 6-trinitronaphthalene by deamination using Hodgson and Turner's [4] or Hodgson and Birtwell's method [5] gave complex mixtures from which only 4 : 7-dinitro-2-naphthol could be isolated, even by chromatography. In Sandmeyer reactions the only identifiable material was 1-diazo-4 : 7-dinitro-2-naphthol.

Bromination of 2 : 7- *and* 4 : 7-*Dinitro*-1-*naphthylamines and Attempted Bromination of* 2 : 4 : 7-*Trinitro*-1-*naphthylamine*.—The amine (0·1 g.) was dissolved in pyridine (7 c.c.) and to this was added a 1 : 10 w/v solution of bromine (2 mols) in pyridine (1·5 c.c.). After 2 days the precipitate of almost pure bromodinitronaphthylamine was collected, washed with ether, and crystallised from hot ethanol; 4-*bromo*-2 : 7-*dinitro*-1-*naphthylamine* had m. p. 272° (Found : C, 38·0; H, 1·9; Br, 26·7. $C_{10}H_6O_4N_3Br$ requires C, 38·5; H, 1·9; Br, 25·6%); 2-bromo-4 : 7-dinitro-1-naphthylamine had m. p. 278° (Found : C, 39·0; H, 1·7; Br, 25·1%). Further amounts of products were obtained by pouring the original filtrates into dilute hydrochloric acid (combined yields *ca.* 70%). The trinitroamine was recovered unchanged.

1 : 2 : 4-*Tribromo*-7-*nitronaphthalene* was obtained by diazotising 2 : 4-dibromo-7-nitro-1-naphthylamine by Hodgson and Walker's method [19] and a subsequent Sandmeyer reaction (cf. the behaviour of diazotised 2 : 4 : 7-trinitro-1-naphthylamine) in 50% yield; crystallised from ethanol it had m. p. 183° (Found : C, 29·3; H, 0·98; Br, 56·8. $C_{10}H_4O_2NBr_3$ requires C, 29·3; H, 0·98; Br, 58·5%).

1 : 4 : 6-*Trinitronaphthalene and Attempted Preparation of* 1 : 2 : 7-*Trinitronaphthalene*.—4 : 7-Dinitro-1-naphthylamine (1·5 g.) was dissolved in sulphuric acid (*d* 1·84; 1·5 c.c.) and added to a solution of sodium nitrite (0·6 g.) in sulphuric acid (*d* 1·84; 3·0 c.c.). The mixture was added to acetic acid (9 c.c.) below 20° and after 30 min. ice-cold dry ether was added (20 c.c. quickly, then 80 c.c. slowly), precipitating an oil which started to solidify. The top layer was decanted from the pasty mass, and dry ethanol (10 c.c.) stirred in; after a further 15 min. the solid diazonium sulphate (2·4 g.) was collected. This was made into a slurry with water (20 c.c.) and added to the freshly prepared decomposition medium with vigorous stirring, the latter having been prepared by mixing solutions of copper sulphate crystals (10 g.) in water (100 c.c.) and of crystalline sodium sulphite (10 g.) in water (100 c.c.) and then just before use adding sodium nitrite (30 g.). After 15 min. the product was collected, washed with water, dried, and extracted with hot alcohol (100 c.c.); the extract was refluxed with charcoal, filtered, and concentrated, to give crude 1 : 4 : 6-*trinitronaphthalene* (0·3 g., *ca.* 40%; m. p. 97°); recrystallised from alcohol (charcoal) it formed almost white needles, m. p. 113—114° (Found : N, 16·3. $C_{10}H_5O_6N_3$ requires N, 16·0%). In a similar experiment 2 : 7-dinitro-1-naphthylamine failed to yield a solid diazonium sulphate, but the oily precipitate (cf. Ward and Coulson [20]) was decomposed as above, yielding a complex product from which no trinitronaphthalene could be isolated even by chromatography.

Further Nitration of 1 : 4 : 6-*Trinitronaphthalene* (By J. G. Hawkins).—To the trinitronaphthalene (1·0 g.) suspended in sulphuric acid (*d* 1·84; 5 c.c.) was added, during 5 min., nitric acid (*d* 1·5; 2·5 c.c., 15 mols.) and the temperature then raised to 80°, kept there for 3 min., then between 70—75° for 1 hr. After 30 min. at 0° the solids were collected, and washed with ice-cold aqueous sulphuric acid (1 : 1 v/v; 4 × 1 c.c.), and then with water (yield 0·67 g., 60%; m. p. 191—193°), identified as slightly impure 1 : 3 : 5 : 8-tetranitronaphthalene by mixed m. p. and infrared spectra. Pouring the original filtrate on ice-water gave a small amount of low-melting material.

1 : 3 : 5-Trinitronaphthalene was prepared (by T. M. Coulson) in *ca.* 60% yield from diazotised 3 : 5-dinitro-1-naphthylamine by a procedure similar to that used by Ward and

[19] Hodgson and Walker, *J.*, 1933, 1620.

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Coulson [20] to make 1 : 2 : 3 : 4-tetrahydro-6 : 7-dinitronaphthalene. After crystallisation from ethanol it had m. p. 119—121° (Found: C, 46·1; H, 2·0. Calc. for $C_{10}H_5O_6N_3$: C, 45·6; H, 1·9%) (Dimroth and Ruck [13] give 119·5°) alone or mixed with 1 : 3 : 5-trinitronaphthalene prepared from 1 : 5-dinitronaphthalene; [13,21] infrared spectra of the molecular complexes with β-naphthol were also identical.

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[*Received, January 14th*, 1957.]

[20] Ward and Coulson, *J.*, 1954, 4545.
[21] Day, Thesis, London, 1952.

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512. *Perfluoroalkyl Derivatives of Sulphur. Part VI.* Perfluoroalkanesulphonic Acids* $CF_3{\cdot}[CF_2]_n{\cdot}SO_3H$ (n = 1—7).†

By T. GRAMSTAD and R. N. HASZELDINE.

Electrolysis of solutions of alkanesulphonyl chlorides $CH_3{\cdot}[CH_2]_n{\cdot}SO_2Cl$ (n = 1—7) in anhydrous hydrogen fluoride gives the perfluoroalkanesulphonyl fluorides $CF_3{\cdot}[CF_2]_n{\cdot}SO_2F$ in 25—80% yield; the fluorides are readily converted into the corresponding sulphonic acids $CF_3{\cdot}[CF_2]_n{\cdot}SO_3H$. Certain of the by-products from the electrolysis of *n*-octanesulphonyl chloride have been identified.

Salts and other derivatives of the acids have been prepared, and a survey has been made of the chemical and physical properties of these compounds.

A GENERAL method for the preparation of the acid fluorides of perfluoroalkanesulphonic acids by electrolysis of the corresponding alkanesulphonyl chloride or fluoride was described in Part IV [1] and exemplified by trifluoromethanesulphonic acid. Preparation of the homologues containing 2—8 carbon atoms is now recorded. Since this work was completed a patent [2] has dealt with related studies (cf. the Experimental part below).

Electrochemical fluorination of an alkanesulphonyl chloride gives smoothly the perfluoroalkanesulphonyl fluoride, which can be converted into the corresponding acid:

$$CH_3{\cdot}[CH_2]_n{\cdot}SO_2Cl \longrightarrow CF_3{\cdot}[CF_2]_n{\cdot}SO_2F \longrightarrow CF_3{\cdot}[CF_2]_n{\cdot}SO_3K \longrightarrow CF_3{\cdot}[CF_2]_n{\cdot}SO_3H$$

The yield of trifluoromethanesulphonyl fluoride by this procedure was 87% [1] and, as expected, the yield decreases steadily as the chain length is increased (79% for perfluoroethane- to 25% for perfluoro-octane-sulphonyl fluoride). The breakdown products from the electrochemical fluorination of *n*-octanesulphonyl chloride contained $CF_3{\cdot}[CF_2]_{0-6}{\cdot}SO_2F$, C_8F_{18}, C_4F_{10}, C_3F_8, C_2F_6, SO_2F_2, SF_6, and $CF_3{\cdot}[CF_2]_{2-5}{\cdot}CO_2H$, formed mainly by carbon–sulphur fission to give perfluoro-octane, which is a major product, and then by carbon–carbon fission: the low yield of perfluoroalkanesulphonic acids containing 1—7 carbon atoms shows, however, that carbon–carbon fission can occur without carbon–sulphur fission. The presence of small amounts of perfluoroalkanecarboxylic acids indicates that electrochemical oxidation (*e.g.*, by oxygen, oxygen difluoride, or sulphuryl fluoride) of the fluorocarbon chain occurs, to give perfluoroacyl fluorides, $CF_3{\cdot}[CF_2]_n{\cdot}COF$, which are subsequently hydrolysed by moist air on removal from the electrolysis cell. Material of b. p. much greater than that of perfluoro-octanesulphonyl fluoride was also noted; it was

* Part V, *J.*, 1956, 2684.
† Presented in part at the Amer. Chem. Soc. Meeting, Atlantic City, 1956.

[1] Gramstad and Haszeldine, *J.*, 1956, 173; cf. Haszeldine and Kidd, *J.*, 1954, 4228; 1955, 2901.
[2] Brice and Trott, U.S.P. 2,732,398; *Chem. Abs.*, 1956, 13982.

free from hydrogen and in view of the b. p. it must contain more than 8 carbon atoms. Free-radical formation and combination on the anode surface thus seems probable, *e.g.*,

$$C_8F_{17}\cdot \longrightarrow C_{16}F_{34}; \quad \cdot C_8F_{16}\cdot SO_2F \longrightarrow (C_8F_{16})_2(SO_2F)_2$$

The perfluoroalkanesulphonyl fluorides are quite volatile (*e.g.*, $C_2F_5\cdot SO_2F$, b. p. 8°; $C_8F_{17}\cdot SO_2F$, b. p. 155°) and have the typical odour of a fluorocarbon. They are hydrolysed only very slowly by water, the more slowly with increase in the length of the chain, doubtless because of decreased solubility; thus perfluoro-octanesulphonyl fluoride is only slightly attacked by water at 180° after several days. Direct reaction of the sulphonyl fluoride with ammonia, piperidine, or aniline yields the corresponding amides $C_8F_{17}\cdot SO_2Z$ (*e.g.*, Z = NH_2, piperidino, or NHPh).

Aqueous potassium hydroxide, like aqueous barium hydroxide,[1] hydrolyses a perfluoroalkanesulphonyl fluoride rapidly and quantitatively to the sulphonate. Alkali-metal perfluoroalkanesulphonates containing 1—4 carbon atoms are appreciably soluble in water; those containing 4—8 carbon atoms show decreasing water-solubility, ultimately less than 2% at 25°, and are surface-active. The salts have high melting points (often >300°), and when anhydrous are stable for prolonged periods at 400°; liberation of fluoride becomes important only above 420°. Formation of fluoride could be detected when potassium perfluoro-octanesulphonate was heated with aqueous potassium hydroxide at 270°, but the salt was stable to water alone at 300°.

The perfluoroalkanesulphonic acids are liberated from their salts by 100% sulphuric acid; they are relatively volatile (*e.g.*, $C_2F_5\cdot SO_3H$, b. p. 178°; $C_8F_{17}\cdot SO_3H$, b. p. 258—260°), hygroscopic (yielding initially solid monohydrates) oils or waxy solids. Their solubility in water and polar solvents decreases with increase in chain length; with this is associated an increase in their marked surface-activity. The anhydrous acids are stable at 400° in absence of air, but liberate fluoride at this temperature when moisture is present; an aqueous solution of a perfluoroalkanesulphonic acid is stable at 280°. Concentrated nitric acid fails to liberate fluoride at 160°. Pyrolysis of perfluoropropanesulphonic acid at 500° gives perfluorohexane, pentafluoropropionyl fluoride, and products of complete breakdown; the C–S bond is again the point of weakness, and degradation of the C_3F_7 radical *via* the alkoxy-radical[3] is indicated:

$$C_3F_7\cdot SO_3H \xrightarrow{500^\circ} C_3F_7\cdot + SO_2, SO_2F_2, H_2O, O_2 \ldots$$

$$2C_3F_7\cdot \longrightarrow C_6F_{14}$$

$$C_3F_7\cdot \xrightarrow[SO_2\ etc.]{O_2} C_3F_7\cdot O\cdot \longrightarrow COF_2 + C_2F_5\cdot \xrightarrow[SO_2\ etc.]{O_2} C_2F_5\cdot O\cdot \longrightarrow \text{etc.}$$

$$C_3F_7\cdot O\cdot + C_3F_7\cdot SO_3H \longrightarrow C_3F_7\cdot OH + C_3F_7\cdot SO_2\cdot O\cdot$$

$$C_3F_7\cdot OH \xrightarrow{-HF} C_2F_5\cdot COF \qquad C_3F_7\cdot SO_2\cdot O\cdot \xrightarrow{-SO_2} C_3F_7\cdot O\cdot \longrightarrow \text{etc.}$$

Electrolysis of a solution of a perfluoroalkanesulphonic acid in anhydrous hydrogen fluoride caused explosions, and only a moderate yield of the perfluoroalkanesulphonyl fluoride was obtained. This is in accord with the difficulty experienced earlier[1] with alkanesulphonic acids, and suggests that water is liberated [$2R_F\cdot SO_3H \rightleftharpoons (R_F\cdot SO_2)_2O + H_2O$], ultimately yielding oxygen difluoride, or that an explosive hypofluorite is formed as intermediate:

$$R_F\cdot SO_3H \longrightarrow R_F\cdot SO_2\cdot OF \longrightarrow R_FF, SO_2F_2, CF_4, \text{etc.}$$

$$\downarrow$$

$$R_F\cdot SO_2F + OF_2$$

Perfluoroalkanesulphonic acids are very strong acids, which readily yield organic or inorganic salts by conventional methods. Derivatives of the acids [*e.g.*, $C_8F_{17}\cdot SO_2Cl$,

[3] Francis and Haszeldine, *J.*, 1955, 2151; Barr and Haszeldine, *J.*, 1955, 1881; 1956, 3416.

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$(C_8F_{17}\cdot SO_2)_2O$] have been obtained by standard techniques or by application of the methods described earlier.[1] Apart from the expected increase in surface-activity, the longer-chain perfluoroalkanesulphonic acids closely resemble trifluoromethanesulphonic acid, the properties of which will be described in more detail in Part VII.

Experimental

Electrochemical Fluorination Apparatus.—The apparatus and techniques used were similar to those described earlier.[1] Fresh anhydrous hydrogen fluoride, sodium fluoride pellets, and squares of rubber sheet were used for each experiment, and a short preliminary electrolysis was sufficient to remove traces of water.

Preparation of the Sulphonic Acids $CF_3\cdot[CF_2]_{1-7}\cdot SO_3H$ *by Electrochemical Fluorination of the Compounds* $CH_3\cdot[CH_2]_{1-7}\cdot SO_2Cl$.—The electrolysis cell contained 700 g. of anhydrous hydrogen fluoride. A 5% solution of the alkanesulphonyl chloride (35 g.) in hydrogen fluoride was electrolysed at a constant 5·0 v until the current (average approx. 6—6·5 amp.) fell to less than 2 amp., then the electrolysis was assumed to be complete (20—40 hr.). The product, collected in traps cooled by liquid oxygen and/or drained from the cell, was given a preliminary distillation to isolate a crude perfluoroalkanesulphonyl fluoride fraction which was then redistilled carefully; all other product were discarded. The b. p.s of the pure *perfluoroalkanesulphonyl fluorides* are shown in Table 1. Somewhat higher yields (5—10%) are obtained by electrolysis of the alkanesulphonyl fluorides, but on a laboratory scale this scarcely merits the extra step in the procedure.

Table 1.

Compound	Yield (%)	B. p.	n_D^{25}	Found C (%)	Found *M*	Required C (%)	Required *M*
$C_2F_5\cdot SO_2F$	79	8°	—	11·8	202	11·9	202
$C_3F_7\cdot SO_2F$	68	36	—	14·2	250	14·3	252
$C_4F_9\cdot SO_2F$	58	64	1·281	15·9	301	15·9	302
$C_5F_{11}\cdot SO_2F$	45	90	1·288	17·0	349	17·1	352
$C_6F_{13}\cdot SO_2F$	36	114	1·292	17·7	398	17·9	402
$C_7F_{15}\cdot SO_2F$	31	135	1·297	18·4	446, 447	18·6	452
$C_8F_{17}\cdot SO_2F$	25	155	1·302	See below		—	—

These fluorides were hydrolysed quantitatively by a 20% excess of 10% aqueous potassium hydroxide in a sealed tube at 20° in 15 hr. The potassium salts of the C_2—C_4 acids were isolated by the extraction procedure described earlier; the potassium salts of the C_5—C_8 acids are moderately to sparingly soluble in water and were separated by filtration. Yields were >90%. Thus, in a typical experiment, perfluoro-octanesulphonyl fluoride (3·8 g.) was shaken vigorously at room temperature in a sealed tube with an excess of 10% aqueous potassium hydroxide for 15 hr. Filtration of the white solid produced, and careful washing with cold water and drying *in vacuo* for 48 hr., gave *potassium perfluoro-octanesulphonate* (93%) (Found : C, 17·7; S, 6·0; K, 7·2. $C_8O_3F_{17}SK$ requires C, 17·9; S, 5·9; K, 7·3%), m. p. 285°. Similarly prepared were the *sodium salt* (96%) (Found : C, 18·3; Na, 4·3. $C_8O_3F_{17}SNa$ requires C, 18·4; Na, 4·4%), m. p. 331—332°, the *barium salt* (92%) (Found : Ba, 12·0. $C_{16}O_6F_{34}S_2Ba$ requires Ba, 12·1%), m. p. >330°, and the *silver salt* (91%) (Found : Ag, 17·6. $C_8O_3F_{17}SAg$ requires Ag, 17·8%).

Potassium (Found : K, 16·1. $C_2O_3F_5SK$ requires K, 16·4%), sodium (Found : Na, 10·4. Calc. for $C_2O_3F_5SNa$: Na, 10·3%), *barium* (Found : Ba, 25·1. $C_4O_6F_{10}S_2Ba$ requires Ba, 25·6%), and silver (Found : Ag, 34·9. Calc. for $C_2O_3F_5SAg$: Ag, 35·2%) *perfluoroethanesulphonate* had m. p. 310°, 395°, >350°, and 287° respectively; they are appreciably soluble in ethanol, acetone, and water.

The perfluoroalkanesulphonic acids were prepared from their anhydrous potassium or barium salts by distillation from 100% sulphuric acid as described in Part IV.[1] Isolation of the more volatile acids was relatively easy, but more trouble was experienced with the higher acids, and careful fractionation was necessary to remove traces of sulphuric acid. The b. p.s of the *perfluoroalkanesulphonic acids* are given in Table 2.

Properties of the Perfluoroalkanesulphonic Acids.—The C_2—C_6 perfluoroalkanesulphonic acids, like trifluoromethanesulphonic acid, are colourless oils which fume in moist air and form solid *monohydrates, e.g.*, $C_2F_5\cdot SO_3H,H_2O$ (Found : equiv., 218), $C_3F_7\cdot SO_3H,H_2O$ (Found : equiv. 266), $C_5F_{11}\cdot SO_3H,H_2O$ (Found : equiv., 369) (equiv. required 218, 268, and 368 respectively).

The hydrates are reconverted into the parent sulphonic acids by distillation from sulphuric acid. Perfluoro-heptane- and -octane-sulphonic acid are solids with the typical waxy appearance of long-chain fluorocarbons and perfluoroalkanecarboxylic acids. The C_2 and C_3 acids are miscible with water in all proportions and are readily soluble in ethanol, ether, or acetone; there is immediate chemical reaction with ethanol and a slower reaction, with tar formation, with the last two solvents. The acids are only slightly soluble in benzene and carbon tetrachloride. The C_4, C_5, and C_6 acid show decreased solubility in water, ethanol, etc., and are substantially insoluble in carbon tetrachloride and benzene. The C_7 and C_8 acid have only moderate solubility in water and are markedly surface-active in that solvent.

TABLE 2.

Compound	Yield * (%)	B. p./mm.†	Found C (%)	Found Equiv.	Required C (%)	Required Equiv.
$C_3F_5{\cdot}SO_3H$	90	178°/760 87°/25	11·8	199	12·0	200
$C_3F_7{\cdot}SO_3H$	86	196°/760	14·5	248	14·4	250
$C_4F_9{\cdot}SO_3H$	88	210—212°/760 105°/22	16·1	299	16·0	300
$C_5F_{11}{\cdot}SO_3H$	83	224—226°/760 97°/4	16·9	350	17·1	350
$C_6F_{13}{\cdot}SO_3H$	80	238—239°/760 110°/5	17·8	398	18·0	400
$C_7F_{15}{\cdot}SO_3H$	77	247—249°/760 122°/5	18·6	446	18·7	450
$C_8F_{17}{\cdot}SO_3H$	70	258—260°/760 145°/10	19·2	499	19·2	500

* Yield from perfluoroalkanesulphonyl fluoride. † B. p.'s at atmospheric pressure are open to error, since partial conversion into perfluoroalkanesulphonic anhydrides occurs at these high temperatures.

The anhydrous acids can be heated to 400° in absence of air without appreciable breakdown. Moisture and air decrease the decomposition temperature of the acids. Thus, anhydrous perfluoro-octanesulphonic acid (2·7 g.), heated to 400° for 3 hr., liberated only a trace of fluoride, but a mixture of the acid (1·0 g.) and water (5·0 g.), heated at the same temperature for 3 hr., liberated 17% of the theoretical amount of fluoride; the aqueous solution of the acid was not decomposed at 280° in 20 hr. A mixture of perfluoro-octanesulphonic acid (1·0 g.) and concentrated nitric acid (5·0 ml.) failed to react or liberate fluoride at 160° during 12 hr.; the surface tension of nitric or sulphuric acid is reduced appreciably by the presence of the sulphonic acid. Pyrolysis of anhydrous perfluoropropanesulphonic acid (2·3 g.) in a platinum tube at 500° during 1 hr. gave perfluorohexane (19%), pentafluoropropionyl fluoride (23%), sulphur dioxide, carbonyl fluoride, and sulphuryl fluoride identified spectroscopically, and hydrogen fluoride and unchanged perfluoropropanesulphonic acid (29%).

Electrochemical fluorination of perfluoroethanesulphonic acid (4·7 g.) in anhydrous hydrogen fluoride (700 g.) at 5 v and 5·9 amp. gave perfluoroethanesulphonyl fluoride (56%), hexafluoroethane, carbon tetrafluoride, and sulphuryl fluoride; several explosions occurred during the electrolysis.

The perfluoroalkanesulphonic acids readily form salts by direct neutralisation. The sodium and potassium salts of the C_1, C_2, and C_3 acid are readily soluble in water, and solubility decreases steadily with increase in chain length: $C_5F_{11}{\cdot}SO_3K$, $C_5F_{11}{\cdot}SO_3Na$, $C_6F_{13}{\cdot}SO_3K$, and $C_6F_{13}{\cdot}SO_3Na$ give approximately 3—4%, 3%, 2%, and 1—2% solutions in water at 25°. Further increase in chain length lowers the solubility even further. The surface-active effect of the alkali-metal perfluoro-octanesulphonates is readily detectable even at these low concentrations in water.

Potassium perfluoro-octanesulphonate (0·9 g.), heated to 300° for 8 hr. with water (5 ml.), failed to liberate fluoride. A parallel reaction with 10% aqueous potassium hydroxide (5 ml.) showed that <2% of fluoride was liberated at 200° after 8 hr., and 8% at 270° after 8 hr.

Anhydrous potassium perfluoro-octanesulphonate (1·1 g.) was unaffected at 400° *in vacuo* for 5 hr.; liberation of fluoride was detected after a similar reaction at 430°. Anhydrous silver perfluoro-octanesulphonate (0·9 g.) became light brown at 400° *in vacuo* in the dark during 3 hr., but no volatile products were detected and only a weak fluoride test was given on treatment of

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the solid with water. In general the potassium sodium, lithium, or barium salts of the perfluoroalkanesulphonic acids can be heated to 350—400° without decomposition, and fluoride liberation occurs only above 420°.

Electrochemical Fluorination of n-*Octanesulphonyl Chloride.*—This reaction was investigated more fully. *n*-Octanesulphonyl chloride (30·5 g.) was added to the electrolysis cell to give a 5% solution by weight in hydrogen fluoride (580 g.). Electrolysis was started at 5·0 v and 3·8 amp., and the potential was maintained at 5·0 v throughout. The average current was 6·4 amp. After 44 hr. the current fell to 1·2 amp. and the electrolysis was complete. The product (excluding carbon tetrafluoride and hydrogen chloride) was examined in two portions: *A*, material (28·5 g.) of higher b. p. which collected as a lower layer and was drained from the cell by means of valve *Z*;[2] *B*, more volatile products (28 g.) which were swept from the cell by the hydrogen evolved and collected in traps at −78° and −183°.

Distillation of *A* gave fractions: (i) perfluoro-octane (5·7 g.), b. p. 103—110°, identified by means of its b. p. (103°)[4] and comparison of its infrared spectrum with that of a reference sample made by reaction of *n*-octane with cobalt trifluoride.[4] A small amount (*ca.* 0·3 g.) of perfluorohexanesulphonyl fluoride, b. p. 113°, contaminated the perfluoro-octane but was readily detected by means of the strong asymmetric and symmetric $-SO_2F$ stretching vibrations in the infrared spectrum. (ii) Perfluoro-octanesulphonyl fluoride (17·8 g., 25%) (Found: C, 19·1%; H, 0; *M*, 500, 496. Calc. for $C_8F_{18}O_2S$: C, 19·1%; H, 0; *M*, 502), b. p. 155°, n_D^{20} 1·302. (iii) Polymeric material (3·1 g.), b. p. 100—120°/14 mm. Infrared spectroscopy showed that carbon–hydrogen bonds were absent, and that chains of CF_2 groups were present; SO_2F groups were also present. (iv) A residue (0·9 g.) which solidified.

Distillation of *B in vacuo* gave a series of arbitrary fractions. Infrared spectroscopy, molecular-weight determination, and the b. p. range revealed the presence of (i) $CF_3{\cdot}[CF_2]_{4-6}{\cdot}SO_2F$ (2·2 g.), b. p. 80—98° and 105—140°, (ii) $CF_3{\cdot}[CF_2]_{1-3}{\cdot}SO_2F$ (2·1 g.), b. p. 0—80°, (iii) $CF_3{\cdot}SO_2F$ (0·7 g.), b. p. *ca.* −20°, (iv) perfluoroalkanecarboxylic acids $CF_3{\cdot}[CF_2]_{2-5}{\cdot}CO_2H$ (0·3 g.), originally mixed with fractions (i) and (ii), but easily detected by means of the infrared carbonyl stretching vibration and separated from the sulphonyl fluorides by their preferential solubility in ice-water (5 g.) (neutralisation of the aqueous extract with aqueous sodium hydroxide and freeze-drying of the solution gave the mixed sodium salts $CF_3{\cdot}[CF_2]_{2-5}{\cdot}CO_2Na$ identified by means of their infrared spectra), (v) perfluoro-octane (7·4 g.), b. p. 98—105°, identified by means of its infrared spectrum, (vi) perfluoro-butane (0·7 g.), -propane (0·7 g.), and -ethane (1·0 g.), as a mixture analysed spectroscopically, (vii) sulphuryl fluoride (4·0 g.), (viii) sulphur hexafluoride (1·3 g.), and (ix) unidentified material (5·9 g.), probably containing other fluorocarbons. Hydrogen chloride was removed from fractions (vi)—(ix) by washing with water before distillation.

Fractions *B*(i) and (ii) were examined further. Gas–liquid chromatography (5 mg. samples on to a 10′ column, 1/4″ int. diam., packed with 40—80 mesh Celite containing 30% of dinonyl phthalate; nitrogen flow 2 l./hr.; 20°) showed qualitatively that *B*(i) contained three components in approximately equal amounts. A 5 mg. portion of *B*(i) was then added to the column, and the three fractions were collected separately in traps cooled by liquid oxygen; this was repeated five times. The fractions were then identified by their b. p.s (isoteniscope) and molecular weights. *B*(ii) was similarly treated and shown to contain three components in approximately equal amounts. The results are shown in Table 3. The b. p.s and molecular

TABLE 3.

Fraction	Wt. (g.)	$CF_3{\cdot}[CF_2]_n{\cdot}SO_2F$ *n*	B. p.	*M*	Fraction	Wt. (g.)	$CF_3{\cdot}[CF_2]_n{\cdot}SO_2F$ *n*	B. p.	*M*
B(i)	0·7	4	90°	345	*B*(ii)	0·7	1	8°	202
B(i)	0·7	5	115	399	*B*(ii)	0·7	2	35	244
B(i)	0·7	6	136	448	*B*(ii)	0·7	3	65	297

weights should be compared with those of the analysed perfluoroalkanesulphonyl fluorides (Table 1).

The above procedure thus shows that approximate yields of products from the electrochemical fluorination of octanesulphonyl chloride are $C_8F_{17}{\cdot}SO_2F$ (25%); $CF_3{\cdot}[CF_2]_{0-6}{\cdot}SO_2F$ (approx. 1·5% each; 9% total); $CF_3{\cdot}[CF_2]_{2-5}{\cdot}CO_2H$ (1%); C_8F_{18} (21%); C_4F_{10} (1%); C_3F_8

[4] Haszeldine and Smith, *J.*, 1950, 2619, 2787, 3617; 1951, 603.

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(1%); C_2F_6 (1·5%); SO_2F_2 (23%); SF_6 (6%). Carbon tetrafluoride and unidentified material account for most of the missing product.

Derivatives of Perfluoro-octanesulphonic Acid.—The inorganic salts have been described above. The S-*benzylthiuronium salt* (Found: C, 28·5; H, 1·9. $C_{16}H_{11}O_3N_2F_{17}S_2$ requires C, 28·8; H, 1·7%) has m. p. 112—113° (from aqueous ethanol).

(a) *Amides.* Perfluoro-octanesulphonyl fluoride (1·3 g.), an excess of anhydrous ammonia, and anhydrous ether (1 ml.) were allowed to warm from −40° to room temperature overnight. Anhydrous ether (15 ml.) was added to the white solid produced to dissolve the amide; the ammonium fluoride was filtered off, and the extraction was repeated with the solid obtained by evaporation of the filtrate to dryness *in vacuo*. The crude amide, m. p. 149—150°, was recrystallised three times from chloroform, to give perfluoro-octanesulphonamide (85%) (Found: C, 19·1; H, 0·5; N, 2·8. Calc. for $C_8H_2O_2NSF_{17}$: C, 19·2; H, 0·4; N, 2·8%), m. p. 152°. The amide has an acid reaction in aqueous solution and liberates carbon dioxide from concentrated aqueous sodium hydrogen carbonate.

Reaction of perfluoro-octanesulphonyl fluoride (1·0 g.) with a 10% excess of piperidine at 100° for 4 hr., followed by ether-extraction, etc., gave the *piperidide* (78%) (Found: C, 27·2; H, 1·8; N, 2·5. $C_{13}H_{10}O_2NSF_{17}$ requires C, 27·5; H, 1·7; N, 2·5%), m. p. 77° (from chloroform).

The *anilide* (Found: C, 29·1; H, 1·1; N, 2·5. $C_{14}H_6O_2NSF_{17}$ requires C, 29·2; H, 1·0; N, 2·4%), m. p. 102° (from benzene), was similarly prepared in 70% yield by reaction of perfluoro-octanesulphonyl fluoride (1·3 g.) with aniline at 100° for 8 hr.

(b) *Perfluoro-octanesulphonyl chloride.* The sulphonic acid (4·1 g.) and a three-fold excess of phosphorus pentachloride were heated *in vacuo* at 120° for 4 hr., then heated with a free flame to distil out the crude sulphonyl chloride, b. p. 180—210°. This was redistilled *in vacuo* then again at atmospheric pressure, to give *perfluoro-octanesulphonyl chloride* (78%) (Found: C, 18·4. $C_8O_2SClF_{17}$ requires C, 18·5%), b. p. 194—195°, n_D^{20} 1·324. When treated with anhydrous ammonia and ether it yields perfluoro-octanesulphonamide identical with the material described above. The anilide (see above) is more readily prepared by use of the sulphonyl chloride than by use of the sulphonyl fluoride.

(c) *Perfluoro-octanesulphonic anhydride.* Perfluoro-octanesulphonic acid (5·3 g.) was mixed with a six-fold excess of phosphoric oxide, kept at 100° for 4 hr., then heated *in vacuo* with a free flame to distil out the crude anhydride, b. p. 100—120°/*ca.* 10^{-3} mm.; cautious even heating must be applied to prevent extensive charring and frothing. Redistillation *in vacuo* and again at 760 mm. gave *perfluoro-octanesulphonic anhydride* (63%) (Found: C, 19·4%; equiv., 978, 979. $C_{16}O_5F_{34}S_2$ requires C, 19·5%; equiv., 982), b. p. 269—270°.

(d) *Perfluoro-octanesulphonyl fluoride.* The acid fluoride (1·8 g.), heated with water (3 ml.) at 180° in a sealed tube for 3 days, underwent 10% hydrolysis. In a parallel experiment with 50% aqueous dioxan as solvent, extensive reaction of the perfluoro-octanesulphonyl fluoride occurred, but this was accompanied by attack on the dioxan to give tarry products.

Since this work was completed some of the compounds described above have been reported by Brice and Trott,[2] in some instances without analytical data. In general, however, there is satifactory agreement with our results: $C_2F_5{\cdot}SO_2F$, b. p. 7·5°; $C_2F_5{\cdot}SO_3H$, b. p. 175°; $C_2F_5{\cdot}SO_3M$ (M = Na, Ag); $C_5F_{11}{\cdot}SO_2F$, b. p. 89—91°; $C_5F_{11}{\cdot}SO_3K$; $C_6F_{13}{\cdot}SO_2F$, b. p. 114—115°; $C_6F_{13}{\cdot}SO_3H$, b. p. 95/3·5 mm.; $C_8F_{17}{\cdot}SO_2F$, b. p. 154·5°/744 mm.; $C_8F_{17}{\cdot}SO_3K$; $(C_8F_{17}{\cdot}SO_2)_2O$, b. p. 260—275°; $C_8F_{17}{\cdot}SO_2Cl$, b. p. 194°; $C_8F_{17}{\cdot}SO_2{\cdot}NH_2$, m. p. 151—152°.

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University Chemical Laboratory, Cambridge. [*Received, February 25th,* 1957.]

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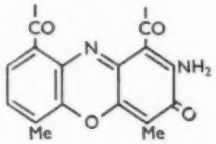
513. *The Chemistry of Mould Metabolites. Part II.* A Partial Structure for Polystictin.*

By G. W. K. Cavill, P. S. Clezy, and J. R. Tetaz.

Degradative and spectroscopic studies on polystictin (cinnabarin), a red pigment isolated from *Coriolus sanguineus* (Fr.), show the presence of a phenoxazone nucleus. The quinonoid ring is substituted by an acidic hydroxyl and an amino-group, and the benzenoid ring is believed to contain the uncharacterised moiety ($C_2H_2O_2$). A 1-amino-2-hydroxyphenoxazin-3-one structure is proposed for the chromophore.

Polystictin, $C_{14}H_{10}O_5N_2$, a red pigment isolated from the wood-rotting fungus *Coriolus sanguineus*,[1,2] has been identified with cinnabarin, isolated from *Trametes cinnabarina*.[3] Previous work [2] indicated the presence of an acidic hydroxyl group, an amide group, possibly an ether link, and an unsaturated nucleus containing a quinonoid system and heterocyclic nitrogen. These observations are now supported by degradative evidence,[4] but the amide group is modified to a vinylogous amide system, ·CO·C:C·NH_2.

Polystictin or *O*-methylpolystictin with potassium permanganate or with alkaline hydrogen peroxide yields oxalic acid and ammonia.[5] Such complete breakdown is characteristic of highly substituted quinones but attempts to convert polystictin into a stable derivative of the quinol, suitable for oxidation, failed. Hydrogenation (palladium catalyst) of *O*-methylpolystictin gives a dihydro-derivative, which is rapidly re-oxidised in air. A trace of a reduced methylated substance, insufficient for degradation, was isolated on treatment of *O*-methylpolystictin with dimethyl sulphate in alkaline solution containing an excess of zinc dust.



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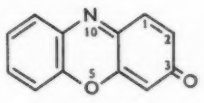

(II)

Fusion of polystictin with a mixture of zinc dust, zinc chloride, and sodium chloride was attempted in expectation that the quinone would be converted into the parent carbocyclic (or heterocyclic) system.[6] However, a yellow oil was isolated which, on chromatography, gave an orange substance (H) in <0·1% yield, with other, unidentified products. The ultraviolet absorptions of polystictin and its derivatives (see Table) are similar to that of actinomycin,[7,8] which has the chromophore (I), and the changes in absorption of actinomycin caused by cold aqueous alkali are also shown by *O*-methylpolystictin.[9] The ultraviolet absorption of product H is very similar to that of phenoxazin-3-one (II), although insufficient was available for determination of accurate ε values; and the R_F values of product H and phenoxazin-3-one, in various solvent systems, are identical: hence product H is considered to be phenoxazin-3-one. The infrared spectrum ("Nujol"

* Part I, *J.*, 1953, 525.

[1] Report Nat. Health Med. Res. Council Australia, 1946, p. 12; Lemberg, *Austral. J. Exp. Biol. Med. Sci.*, 1952, **30**, 271.
[2] Cavill, Ralph, Tetaz, and Werner, *J.*, 1953, 525.
[3] Gripenberg, *Acta Chem. Scand.*, 1951, **5**, 590.
[4] Cf. Cavill and Tetaz, *Chem. and Ind.*, 1956, 986.
[5] Cf. Tetaz, Ph.D. Thesis, N.S.W. University of Technology, 1955.
[6] Cf. Clar, *Ber.*, 1939, **72**, 1645.
[7] Brockmann and Muxfeldt, *Chem. Ber.*, 1956, **89**, 1397; *Angew. Chem.*, 1956, **68**, 69.
[8] Angyal, Bullock, Hanger, and Johnson, *Chem. and Ind.*, 1955, 1295.
[9] Personal communication from Professor S. J. Angyal.

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mull) of product H, whilst showing no bands in the 3 μ region attributable to hydroxyl or amino-groups (cf. polystictin),[2] shows strong absorption at 1644 and 1620 cm.$^{-1}$; these bands, also present in the spectrum of phenoxazin-3-one, are assigned to >C=O and >C=N– groups. Isolation of a quinonoid product by zinc dust degradation is unusual.

The hydroxyl group in polystictin was previously placed [2] *peri* to a carbonyl system on the basis of colour reactions. However, the strong absorption at 3505 cm.$^{-1}$ in polystictin,

Ultraviolet absorption spectra of polystictin and related compounds.

Compound *	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ) †	log ε	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε
Polystictin (EtOH)	225		~270		—		430 445—450	
(dioxan)	234	4·2	~260	3·9	—		430 455	4·0 4·0
Actinomycin (*a*) [7]	238		Infl.		—		425 443	
(*b*) [8]	232—236	4·50			—		443—444	4·33
2-Hydroxyphenoxazin-3-one	223	4·20	~260		—		400	4·09
2-Aminophenoxazin-3-one	237	4·17	268	3·90	—		421—436	4·10
O-Methylpolystictin	234	4·65	265	4·30	310—315	3·59	434	4·55
O-Acetylpolystictin	232	4·61	260	4·30	305	3·53	433	4·39
N-Acetyl-*O*-methylpolystictin	236	4·46	265	4·13	310	3·42	434	4·37
Phenoxazin-3-one	245	4·13	263	3·89	348	3·99	449	3·94
Product H	247		~260—270		350		445—450	
Triacetylanhydrodihydro-polystictin	245	4·52	—		320	3·48	433	3·97
Triacetyldihydro-*O*-methyl-polystictin	235	4·57	—		315	3·55	405	3·86
Reduced methylated poly-stictin	235		—		330		398	
Diacetyl*iso*polystictin	225	4·38	260	4·11	Infl.		393	4·24
Diacetyl-*O*-methyl*iso*poly-stictin	237	4·48	245 265	4·41 4·09	Infl.		404	4·40

* In ethanol (95%) unless otherwise stated.
† Inflexions.

attributable to a weakly hydrogen-bonded, or a non-bonded, hydroxyl group is not shown by *peri*-hydroxyquinones,[10] and hence the hydroxyl group is now placed on the quinonoid ring of the phenoxazone, in which position it also accommodates the known acidity of polystictin.

The formation of ammonia on alkaline hydrolysis of polystictin, together with the subsequent evolution of carbon dioxide on acidification, suggested the presence of an amide (or imide) grouping, an observation supported by infrared spectroscopic data; but we failed to prove the presence of an amide group by dehydration to the nitrile (cf. terramycin [11]). The ready liberation of ammonia on hydrolysis, by 2N-hydrochloric acid, of polystictin and *O*-methylpolystictin, together with the isolation of an acidic methylated substance ($C_{15}H_{11}O_6N$) as a hydrolytic by-product of the methylation of polystictin,[2] indicates the presence of an aminoquinonoid or similar system. That is, polystictin may contain a vinylogous rather than a simple amide. Further, acetylation of the amino-group explains the conversion of *O*-methylpolystictin into *N*-acetyl-*O*-methylpolystictin and, more significantly, explains the formation of triacetyldihydro- rather than diacetyldihydro-compounds on reductive acetylation of polystictin and its derivatives.[2]

The orientation of the amino- and hydroxy-substituents on the phenoxazone nucleus is shown by reductive acetylation. In the conversion of polystictin and *O*-acetylpolystictin into triacetylanhydrodihydropolystictin, and of *O*-methylpolystictin and *N*-acetyl-*O*-methylpolystictin into triacetyldihydro-*O*-methylpolystictin, two acetyl groups are

[10] Flett, *J.*, 1948, 1441.
[11] Hochstein, Stephens, Conover, Regna, Pasternack, Gordon, Pilgrim, Brunings, and Woodward, *J. Amer. Chem. Soc.*, 1953, **75**, 5455.

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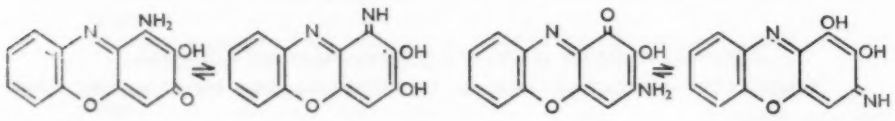
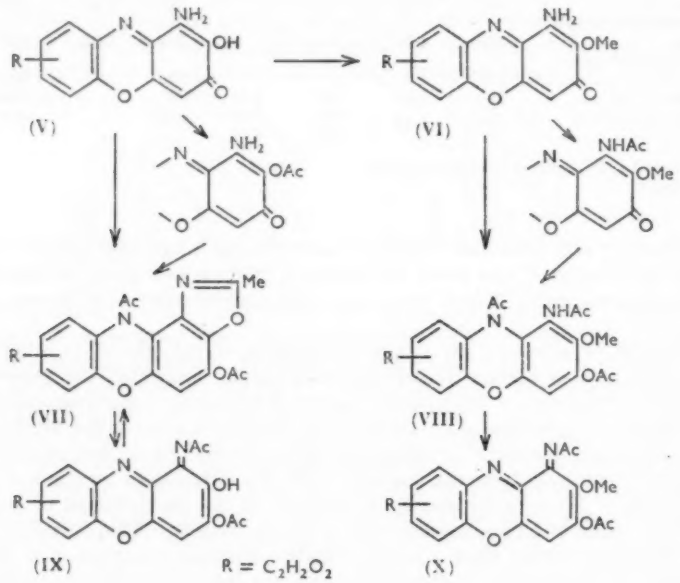
involved in the reductive acetylation of the phenoxazone nucleus and the third is present on the amino-group. The anhydro-compound obtained from polystictin and from *O*-acetylpolystictin is thus an oxazole, formed by cyclisation of the acetamido-substituent with an adjacent hydroxyl (or acetate) group. As *O*-methylpolystictin and its *N*-acetyl derivative do not form an anhydro-compound, the hydroxyl group involved in the above



(III) (IIIa) (IV) (IVa)

cyclisation must be that originally present in polystictin. Further, the original amino-substituent, thus placed *ortho* to the acidic hydroxyl group on the phenoxazone nucleus, cannot be adjacent to the quinone carbonyl group (a potential hydroxyl group). Hence the chromophore of polystictin is represented by structure (III) or (IV).

It is most likely that the pyruvic acid (0·4 mol.), obtained by the action of hot 25% sodium hydroxide solution on polystictin, arises from the breakdown of this trisubstituted quinonoid ring.[12]



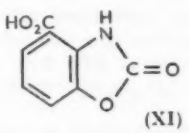
(V) (VI) (VII) (VIII) (IX) (X) R = $C_2H_2O_2$

Whilst the isolation of phenoxazin-3-one (II), on zinc dust distillation, supports the *para*-quinonoid structure (III) for the chromophore of polystictin, the *ortho*-structure (IV) cannot be excluded; a compound of type (IV) could be degraded *via* the tautomeric dihydroxy-*para*-quinone imine (IVa). However, the striking similarity in the ultraviolet absorption spectra of polystictin, of actinomycin (cf. I), and of 2-amino- and 2-hydroxy-phenoxazin-3-one strongly supports the *para*-quinonoid structure (III). Polystictin is

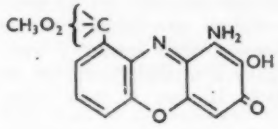
[12] Cf. Asano and Yamaguti, *J. Pharm. Soc. Japan*, 1940, **60**, 585.

then represented by (V; R = $C_2H_2O_2$), *O*-methylpolystictin by (VI), and the reduced acetylated derivatives by (VII) and (VIII), respectively.

Oxidation of triacetylanhydrodihydro- (VII) and of triacetyldihydro-*O*-methylpolystictin (VIII) with nitrous acid in dilute hydrochloric acid yields an acidic diacetyl*iso*polystictin (IX) (with the re-addition of the elements of water) and a neutral diacetyl-*O*-methyl*iso*polystictin (X), respectively. The acetyl group lost during this oxidation of the reduced acetylated derivatives (VII and VIII) must be that attached to the ring-nitrogen atom (cf. Brockmann and Franck [13]) and hence the new quinonoid compounds (IX and X), which retain two acetyl groups, are formulated as derivatives of the tautomeric *iso*polystictin (IIIa). These reactions require the amino-group to be *ortho* (or *para*) to the ring-nitrogen atom and hence provide additional confirmation of the *meta*-relation of the amino-group to the quinone-carbonyl group. Diacetyl*iso*polystictin (IX), which is also obtained as a by-product during the working-up of the triacetylanhydrodihydro-derivative (VII), should be identical with Gripenberg's cinnabarin *leuco*acetate A[3] (compare m. p. and acidity). However, cinnabarin *leuco*acetate A was acetylated to yield the *leuco*acetate B, identical with triacetylanhydrodihydropolystictin (VII), whereas the compound (IX) requires reductive acetylation to reform the oxazole (VII).



(XI)



(XII)

An uncharacterised moiety ($C_2H_2O_2$), substituted on the benzene ring, appears not to have been involved in any of the above reactions. Gripenberg, Honkanen, and Patoharju [14] reported the isolation of benzoxazolone-4-carboxylic acid (XI) on permanganate oxidation of cinnabarin (polystictin) (cf. the analogous formation of 7-methylbenzoxazolone-4-carboxylic acid from actinomycin [8]). Thus the $C_2H_2O_2$ fragment is attached at the 9-position on the phenoxazone nucleus, and polystictin is represented by the partial structure (XII).

Experimental

Light petroleum had b. p. 60—80°. Alumina refers to aluminium oxide of grade H from Peter Spence. Neutralised alumina is prepared by washing grade H alumina with methanol–acetic acid (9 : 1), triturating it with hot methanol until all washings are neutral, and drying it at 150—200°. Carbon, hydrogen and nitrogen microanalyses are by Dr. E. Challen and Mr. D. Weeden of this University, additional microanalyses by C.S.I.R.O. Microanalytical Laboratory (Melbourne), and infrared spectra by Mr. I. H. Reece.

Molecular Weight of Polystictin and its Derivatives.—Low solubility of polystictin, and many of its derivatives, in organic solvents hinders molecular-weight determination. No satisfactory determination has been possible for polystictin. However, an ebullioscopic estimation on *O*-methylpolystictin (28·15 mg.) in chloroform (5 ml.) gave a b. p. elevation of 0·055° (Found : *M*, 254. Calc. for $C_{15}H_{12}O_5N_2$: *M*, 300). Isothermic microdistillation [15] of triacetyldihydro-*O*-methylpolystictin, in acetone, was undertaken because of a wide discrepancy in the results of Rast determinations (Found : *M*, 454. Calc. for $C_{21}H_{20}O_8N_2$: *M*, 428). These results confirm the formula $C_{14}H_{10}O_5N_2$ for the parent compound. In agreement with Lemberg,[1] we have found Rast determinations on triacetylanhydrodihydropolystictin (Gripenberg's [3] cinnabarin *leuco*acetate B) to be unreliable.

Oxidation of O-*Methylpolystictin with Potassium Permanganate.*—*O*-Methylpolystictin (0·3 g.)

[13] Brockmann and Franck, *Angew. Chem.*, 1956, **68**, 68.
[14] Gripenberg, Honkanen, and Patoharju, *Chem. and Ind.*, 1956, 1505.
[15] Niederl, Kasanof, Kisch, and Subba Rao, *Mikrochem.*, 1949, **34**, 132.

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and potassium permanganate (1 g.) were dissolved in acetone (300 ml.) and kept for 48 hr. at 0—10°. The precipitated manganese dioxide was then filtered off and, after trituration with saturated sodium hydrogen carbonate solution, rejected. The alkaline washings, after acidification with 2N-hydrochloric acid, were extracted with chloroform. Removal of solvent gave a buff solid (11 mg.), which was shown by paper chromatography [16] to be a mixture of unidentified acids. The aqueous solution remaining after chloroform extraction was evaporated; the residue, sublimed at 160—170°/1 mm., gave oxalic acid (20 mg.), m. p. and mixed m. p. 98—99°. A further sublimate (6 mg.), m. p. >320°, gave a positive test with Nessler's reagent, indicating ammonium chloride.

Oxidation of Polystictin with Alkaline Hydrogen Peroxide Solution.—Polystictin (0·2 g.) in 0·3% aqueous sodium hydroxide solution (60 ml.) was treated with 30% hydrogen peroxide (2 ml.) and kept for 1 week at room temperature, hydrogen peroxide (1 ml.) being added every second day. The colour changed from violet to pale yellow and the pH from 10—11 to 8. No basic products were isolated from the alkaline solution. After acidification with hydrochloric acid, the solution was continuously extracted with ether. Paper chromatography of this extract with ethyl methyl ketone–cineole–53% w/v formic acid (50 : 50 : 36),[17] and ethanol–water–ammonia (*d* 0·88) (80 : 16 : 4) [18] as solvent systems revealed a mixture of acids. The spots were developed with silver nitrate.[17] One had R_F 0·51, identical with that of oxalic acid.[17]

Hydrogenation of O-*Methylpolystictin.*—*O*-Methylpolystictin (100 mg.) in acetic acid (15 ml.) was reduced over palladium–charcoal for 35 min. at N.T.P., 0·84 mol. of hydrogen being absorbed. The amber solution, after removal of catalyst, was neutralised with excess of sodium hydrogen carbonate solution, then extracted with chloroform (2 × 100 ml.). The orange-brown solid obtained gave *O*-methylpolystictin (64 mg.), m. p. 234—240° (decomp.), from ethanol (Found: C, 60·2; H, 4·0; N, 9·65. Calc. for $C_{15}H_{12}O_5N_2$: C, 60·0; H, 4·0; N, 9·3%).

Reductive Methylation of O-*Methylpolystictin.*—*O*-Methylpolystictin (0·1 g.) and zinc dust (3 g.) were suspended in cold aqueous 2N-sodium hydroxide (10 ml.) and shaken with dimethyl sulphate (2 ml.) for 15 min. After filtration, the yellow solution was extracted with chloroform (60 ml.), and the aqueous layer rejected. Removal of solvent gave a brown oil (44 mg.), purified by chromatography on alumina from light petroleum. The yellow band, eluted with chloroform, yielded a yellow substance (4 mg.), m. p. 188—190° (decomp.) (from benzene–light petroleum), which gave the green colour in concentrated sulphuric acid characteristic of the reduced acetylated derivatives of polystictin.[2]

Zinc Dust Fusion of Polystictin.—Polystictin (20 mg.), zinc dust (200 mg.), zinc chloride (400 mg.), and sodium chloride (20 mg.) were fused together at 230—240° for 10 min., with stirring. The products of 85 fusions were combined and digested with N-hydrochloric acid (1 l.) for 1 hr. The remaining amorphous brown solid was filtered off, washed with water, dried at 60°, and extracted (Soxhlet) with chloroform for 24 hr. Similarly, the acid filtrate (and washings) were continuously extracted with ether. The combined product of the two extractions, a yellow oil (100 mg.), was taken up in benzene (50 ml.) and chromatographed on neutralised alumina. An orange-red band eluted with benzene–chloroform (3 : 1) gave a product, purified by distillation at 120—150°/0·15 mm. This substance was further resolved on treatment with hexane. A small quantity of fine red needles (*ca.* 1 mg.) remained, whilst the yellow hexane solution slowly deposited product H (*ca.* 1 mg.), as orange prisms. The red substance, and other fractions obtained during chromatography, are being investigated.

The R_F values of product H and phenoxazin-3-one were identical in 5% aqueous pyridine (R_F 0·53), in *iso*propanol–water–90% formic acid (25 : 65 : 10) (R_F 0·81), and in acetone–water–90% formic acid (10 : 80 : 10) (R_F 0·61), the horizontal technique being used. The spots were detected by their colour and by their orange-pink fluorescence in ultra-violet light.

Acid Hydrolysis of Polystictin and of O-*Methylpolystictin.*—A suspension of polystictin (50 mg.) in 2N-hydrochloric acid (25 ml.) was heated under reflux for 4 hr. On cooling, the mixture was filtered to remove an intractable black precipitate. The red filtrate was diluted with water (100 ml.), the colour changing to pale yellow. A sample of this solution (10 ml.), made alkaline with 2N-sodium hydroxide, gave an orange-yellow precipitate with Nessler's reagent.

O-Methylpolystictin was similarly hydrolysed, ammonia again being detected in the filtrate.

[16] Long, Quayle, and Stedman, *J.*, 1951, 2197.
[17] Anet and Reynolds, *Austral. J. Chem.*, 1955, **8**, 267.

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Acetylation of O-*Methylpolystictin.*—*O*-Methylpolystictin (50 mg.), acetic anhydride (6 ml.), and pyridine (1 ml.) were refluxed for 7 min. The red solution was then poured on ice, and the orange-red solid (55 mg.) precipitated was dissolved in chloroform (200 ml.). This extract, after treatment with 2N-hydrochloric acid (2 × 10 ml.) to remove starting material, gave N-*acetyl*-O-*methylpolystictin*, finally isolated as red needles, m. p. 232° (decomp.) (from benzene) (Found: C, 60·0; H, 4·6; N, 8·4; Ac, 12·7. $C_{17}H_{14}O_6N_2$ requires C, 59·7; H, 4·1; N, 8·2; Ac, 12·7%).

Reductive Acetylation of N-*Acetyl*-O-*methylpolystictin.*—*N*-Acetyl-*O*-methylpolystictin (35 mg.), acetic anhydride (5 ml.), pyridine (2 drops), and an excess of zinc dust were heated together for 5 min. The mixture, on cooling, was poured on ice, and the resultant yellow solid filtered off. Repeated recrystallisation from light petroleum–benzene gave triacetyldihydro-*O*-methylpolystictin (28 mg.) as yellow needles, m. p. and mixed m. p. 157°. (This compound is described in Part I [2] as the product of reductive acetylation of *O*-methylpolystictin.)

Reductive Acetylation of O-*Acetylpolystictin.*—*O*-Acetylpolystictin (25 mg.), reductively acetylated as described for polystictin,[2] gave triacetylanhydrodihydropolystictin (15 mg.), as yellow needles, m. p. 201° (from benzene) (Found: C, 60·2; H, 3·8. Calc. for $C_{20}H_{16}O_7N_2$: C, 60·6; H, 4·1%).

Nitrous Acid Oxidations of Reduced Acetylated Derivatives.—(*a*) To triacetylanhydrodihydropolystictin (0·3 g.) in 90% dioxan (15 ml.) at 0—5°, 10N-hydrochloric acid (1 ml.) was added, then 30% sodium nitrite solution (1 ml.), giving a red colour; gas was evolved. The precipitate (0·21 g.) gave *diacetyliso*polystictin, orange-red needles, m. p. 211—212° (decomp.) (from alcohol) (Found: C, 58·1; H, 4·0; N, 7·7; Ac, 25·8. $C_{18}H_{14}O_7N_2$ requires C, 58·4; H, 3·8; N, 7·6; Ac, 23·4%), soluble in cold saturated sodium hydrogen carbonate solution and recovered therefrom on acidification.

Diacetyl*iso*polystictin (100 mg.), on reduction as above, gave triacetylanhydrodihydropolystictin (76 mg.) as yellow needles, m. p. and mixed m. p. 197—198° (from benzene).

(*b*) Similarly, triacetyldihydro-*O*-methylpolystictin (200 mg.) in 90% alcohol (20 ml.), with 10N-hydrochloric acid (4 ml.), and 10% sodium nitrite solution (4 ml.) gave an orange-red product (140 mg.), from which *diacetyl*-O-*methyliso*polystictin (25 mg.) was obtained as orange needles, m. p. 209° (decomp.) (Found: C, 59·4; H, 4·4; N, 7·0; Ac, 27·0. $C_{19}H_{16}O_7N_2$ requires C, 59·4; H, 4·2; N, 7·3; Ac, 22·5%), from benzene or ethyl acetate.

Alkaline Hydrolysis of Polystictin.—Polystictin (0·63 g.) in 25% sodium hydroxide solution (50 ml.) was steam-distilled. No volatile base could be detected in 1 hr. The alkaline solution was filtered, then extracted with chloroform to give a trace of brown gum (0·015 g.). After acidification with 5N-sulphuric acid, the aqueous solution was treated with an excess of 2 : 4-dinitrophenylhydrazine sulphate solution, and the yellow precipitate was washed and dried (0·26 g.). Pyruvic acid 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 218°, was isolated as yellow-orange plates on recrystallisation from benzene [Found: N, 20·7%; *M* (Rast), 272. Calc. for $C_9H_8O_6N_4$: N, 20·9%; *M*, 268].

Synthesis of Phenoxazinones.—Phenoxazin-3-one [18] [m. p. 203° (decomp.); yield 23%], and its 2-amino- [19] [m. p. 254—256° (decomp.); yield 38%] and 2-hydroxy-derivative [20] [m. p. 260—270° (decomp.); yield 1%] were prepared as described in the literature. Phenoxazin-3-one and 2-aminophenoxazin-3-one were purified by chromatography on neutralised alumina, followed by vacuum-sublimation at 120—140°/0·1 mm. and 195—205°/0·15 mm., respectively. 2-Hydroxyphenoxazin-3-one was purified by vacuum-sublimation at 170—200°/0·2 mm.

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Sydney, Australia. [*Received, January 7th*, 1957.]

[18] Kehrmann and Saager, *Ber.*, 1902, **35**, 341.
[19] Fischer and Jones, *Ber.*, 1894, **27**, 2782.
[20] Diepolder, *Ber.*, 1902, **35**, 2816.

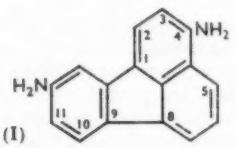
XUM

514. *The Orientation of Fluoranthene-4 : 12-disulphonic Acid.*

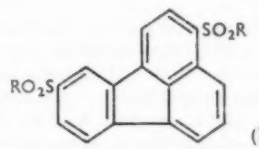
By Th. Holbro and Neil Campbell.

Fluoranthene-4 : 11- and -4 : 12-disulphonanilide have been synthesised. The second substance is identical with that obtained from the disulphonation product of fluoranthene, which is thus fluoranthene-4 : 12-disulphonic acid.[1]

Evidence advanced to show that the product obtained by disulphonation of fluoranthene is the 4 : 12-disulphonic acid [1] is not conclusive since it rests on the assumption that fusion of the acid with sodium hydroxide to give 4 : 12-dihydroxyfluoranthene is unattended by rearrangement. A rigorous proof of the constitution of the acid is now given. 4 : 12-Diaminofluoroanthene [2] (I), when diazotised and treated with sulphur dioxide, gives fluoranthene-4 : 12-disulphonyl chloride (II; R = Cl), which with aniline yields the disulphon-



(I)



(II)

anilide (II; R = NHPh), identical with that obtained from the disulphonation product of fluoranthene. This product is therefore fluoranthene-4 : 12-disulphonic acid (II; R = OH). Comparison of the chromatographic behaviour of the acid with that of naphthalene-2-sulphonic and -2 : 7-disulphonic acid showed that it contained a little monosulphonic acid and a trace of fluoranthene.

Fluoranthene-4 : 11-disulphonanilide has been synthesised from 4 : 11-diaminofluoranthene obtained from the corresponding carboxylic acid by the Curtius reaction.

Experimental

Fluoranthene-4 : 12-disulphonanilide.—Heating 4 : 12-diacetamidofluoranthene [2] (4 g.) with 30% hydrochloric acid (100 c.c.) for 2 hr. at 115° gave 4 : 12-diaminofluoranthene dihydrochloride, which was suspended in water (12 c.c.) and 38% hydrochloric acid (25 c.c.) and added in one operation to sodium nitrite (2·5 g.) in water (5 c.c.) at −10°. After 15 min. addition of cooled acetone (100 c.c.) precipitated the tetrazonium salt which was filtered off, washed with acetone, and at 10° added with stirring to a mixture of acetic acid (50 c.c.) saturated with sulphur dioxide, 38% hydrochloric acid (2 c.c.), and cuprous chloride (0·5 g.). The mixture was kept at 10—20° for 10 min., at 40° for 10 min., and at 80° for 10 min., cooled, and mixed with 10% hydrochloric acid (50 c.c.). The disulphonyl chloride which separated was washed with water, and dried in a vacuum at 35° (yield 3·45 g.). The compound was heated for ½ hr. in aniline (20 c.c.) at 95°, diluted with ethanol, and when poured into 10% hydrochloric acid gave *fluoranthene-4 : 12-disulphonanilide*, m. p. 271° (from chlorobenzene) (Found: C, 65·7; H, 4·1; N, 5·4; S, 12·2. $C_{28}H_{20}O_4N_2S_2$ requires C, 65·6; H, 3·9; N, 5·5; S, 12·5%).

Heating sodium fluoranthenedisulphonate with phosphorus pentachloride for 3 hr. at 145° gave the disulphonyl chloride, which (10 g.) was stirred with aniline (50 g.) at 95°. The magma obtained by cooling was stirred with 10% hydrochloric acid, and the crude fluoranthene-4 : 12-disulphonanilide after repeated crystallisation from *o*-dichlorobenzene, aniline, and chlorobenzene had m. p. 273°, undepressed when mixed with a sample prepared as above.

Fluoranthene-4 : 11-disulphonanilide.—Pyridine (18 g.) was added to fluoranthene-4 : 11-dicarboxylic acid (97 g.) in dry *o*-dichlorobenzene (3200 g.) with stirring at 145—155°, and then

[1] Campbell and Keir, *J.*, 1955, 1233.
[2] Campbell, Leadill, and Wilshire, *J.*, 1951, 1404.

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thionyl chloride (82·5 g.) in 10 min. After 20 min. the excess of thionyl chloride was removed by a current of air. Diethylaniline (25 g.) and portions of sodium azide (total 48 g.) in water (132 g.) were added with brisk stirring at 0—5° to the suspension of the acid chloride. 10% Hydrochloric acid (5 g.) was added and the mixture stirred at 0—5° for 7 hr. and at 20—22° for 7 hr. The resulting azide was washed successively with ethanol, water, and ethanol, and then dried as thoroughly as possible at the pump. The azide in toluene (750 g.) was freed from ethanol and water by distilling off toluene (350 g.) at 100—110 mm. The mixture was then heated at atmospheric pressure on the water-bath until reaction set in, the reaction being moderated by cooling if necessary. After ½ hr. on the water-bath the mixture was boiled for ½ hr., then cooled somewhat, absolute ethanol (145 g.) added, and the mixture boiled for 3 hr. Cooling deposited the *dicarbamate* (40 g.), m. p. 234—235° after crystallisation from chlorobenzene (charcoal) (Found : C, 69·9; H, 5·2; N, 7·7. $C_{22}H_{20}O_4N_2$ requires C, 70·2; H, 5·4; N, 7·5%).

The dicarbamate (100 g.) was added during 1 hr. to 73% sulphuric acid (1500 g.) at 130°, preferably after air has been displaced from the reaction vessel by nitrogen. After being stirred at 130—135° for ¾ hr. the mixture was allowed to cool completely without stirring. The disulphate separated, was washed with 60% sulphuric acid, suspended in water, and stirred with ammonia and ice. 4 : 11-*Diaminofluoranthene* separated and its solution in chloroform (1600 c.c.) after treatment with activated charcoal with light petroleum (b. p. 50—70°, 1350 c.c.) gave yellow plates or red matted needles, m. p. 162—163° (40 g.) (Found : C, 82·6; H, 5·5. $C_{16}H_{12}N_2$ requires C, 82·7; H, 5·2%).

The diamine (4·6 g.) in water (20 c.c.) and 20% hydrochloric acid (7 c.c.) was added to 38% hydrochloric acid (40 c.c.), and to the resulting suspension sodium nitrite (3·4 g.) in water (7 c.c.) was added in one operation with stirring at −10°. After 10 min. the solution was added at 0—5° to a mixture of acetic acid (160 c.c.) saturated with sulphur dioxide, 38% hydrochloric acid (7 c.c.), and cuprous chloride (1·6 g.). The mixture was heated for 15 min. to 70°, maintained at 70—80° for ½ hr., and mixed with water (150 c.c.) at 20°. Crude fluoranthene-4 : 11-disulphonyl chloride (6 g.) separated and when heated (1 hr.) with excess of aniline yielded the *disulphonanilide*, m. p. 303—305° after two crystallisations from *o*-dichlorobenzene (Found : C, 65·9; H, 4·0; N, 5·6%).

Chromatographic Behaviour of Fluoranthene-4 : 12-disulphonic Acid, etc.—The sulphonic acids were placed about 1 cm. from the centre of a 15 mm. Whatman No. 1 filter paper which was placed in a desiccator so that the centre of the paper rested on the end of a capillary tube dipping into a tube of the developing solution. A mixture of butanol (40 ml.), ethanol (10 ml.), water (49 ml.), and concentrated aqueous ammonia (1 ml.) was shaken and the butanol layer used as developer, and the aqueous layer placed in the desiccator to saturate the atmosphere. The chromatogram was examined in ultraviolet light; the spots produced showed that the monosulphonic acids travel much more rapidly to the edge of the paper than do the disulphonic acids. The fluoranthenedisulphonic acid was shown to contain only a small amount of monosulphonic acid along with a trace of fluoranthene.

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515. *A Simple Molecular-orbital Treatment of the Hammett ρσ-Equation: Inductive Constants of the Common Substituents.*

By David Peters.

A simple perturbation treatment of the Hückel molecular-orbital method is applied to the σ-constants of the Hammett ρσ equation. A series of inductive constants is deduced for the common substituents.

Several authors [1-5] have discussed the Hammett ρσ equation [6] in terms of the simple Hückel molecular-orbital method. Jaffe [1] has derived the σ-constants of the common monatomic substituents (hydroxy, amino and the halogens; the word "monatomic" is used in this connexion to denote substituents contributing one atomic orbital), solving the secular equations for all values of the heteroatom parameters; a comparison of the results with experiment allows the selection of a unique set of parameters for the heteroatoms. This method is perhaps more precise than that used here,* but it suffers from certain disadvantages: no comparison with the familiar inductive and mesomeric effects of the resonance theory is possible, and the extension of the method in its present form to more complex substituents (nitro, etc.) would require the acquisition of a large amount of experimental data; further, a complex substituent would have several parameters, and, if it is possible to assign only two parameters, an inductive and a mesomeric, to all substituents, the position is enormously simplified. Jaffe [3] has also discussed the σ-values of the heterocyclic nitrogen atom, using a perturbation method.

In the present paper, a different approach from that used by Jaffe [1-3] is adopted, the perturbation method being applied to the common substituents. The above-mentioned difficulties are then avoided, and interesting information concerning the inductive power of these substituents is obtained. That such an approach has real meaning is suggested by the fact that σ-constants are additive.[8]

Method.—The isolated-molecule approximation [9] is used, although discussions of the chemical reactivity of mesomeric systems are more reliable when the localisation method,[9] with its sound theoretical basis in the transition-state theory,[10] is used. The more precise method meets with difficulties, however. Sixma [4] has used such an approach but here, the side chain, the reaction centre, must be incorporated into the basic model to which the calculations are applied. This results in a multiplicity of models and does not emphasise the most important point of the Hammett ρσ equation, that the σ-constants are independent of the structure of the side chain. If the treatment is to be kept as general as possible, the isolated-molecule approximation is required, together with Hammett's original assumption that the substituents act by virtue of their ability to modify the charges at the *meta*- and *para*-positions in the benzene ring.

The relevant conclusions which follow from the application of perturbation methods to the Hückel method are well known.[11,12] To evaluate the mesomeric effect, the hetero-atoms of the substituent are replaced by carbon atoms and the effect of this idealised

* Perturbation methods are not invariably less accurate than the full solution of the secular equations since the self-consistency of the latter method is lost when heteroatoms having coulomb integrals differing from that of carbon are included.[7]

[1] Jaffe, *J. Chem. Phys.*, 1952, **20**, 279.
[2] *Idem*, *ibid.*, p. 778.
[3] *Idem*, *ibid.*, p. 1554.
[4] Sixma, *Rec. Trav. chim.*, 1953, **72**, 673.
[5] Sandorfy, *Bull. Soc. chim.*, 1949, **16**, 615.
[6] Hammett, "Physical Organic Chemistry," McGraw Hill, New York, 1940, chapter 7.
[7] Coulson and Dewar, *Discuss. Faraday Soc.*, 1947, **2**, 54.
[8] Jaffe, *Chem. Rev.*, 1953, **53**, 191.
[9] Brown, *Quart. Rev.*, 1952, **6**, 63.
[10] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3355.
[11] Jaffe, *ibid.*, 1955, **77**, 274.
[12] Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, *A*, **191**, 39; 1948, *A*, **192**, 16.

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substituent on the charge distribution in the benzene ring is calculated.[12, 13, 14] The majority of the substituents listed by Hammett [6] and by Jaffe [8] may be classified according to the number of atomic orbitals—0, 1, 2, or 3 *—which they contribute to the mesomeric system. In no case does the mesomeric effect alter the charge at the *meta*-position and in only one case, the monatomic substituents, does it affect the charge at the *para*-position.† This distinction leads us to separate the substituents into two groups, those contributing 0, 2 or 3 atomic orbitals to the mesomeric system (class a) and those contributing 1 atomic orbital (class b). Table 1 and 2 present the data thus arranged, all taken from Jaffe [8] with the exception of that for the SR_2^+ which is from ref. 15.

TABLE 1. *Class a.*

Substituent	NR_2^+	SR_2^+	NO_2	CN	SO_2Me *	SOMe *
σ_m	+0·95	+1·0	+0·71	+0·68	+0·65	+0·55
σ_p	+0·86	+1·0	+0·78	+0·63	+0·75	+0·57
Substituent	CF_3	COR	CO_2R	CO_2^-	Alkyl	
σ_m	+0·41	+0·35	+0·35	+0·1	−0·05	
σ_p	+0·55	+0·26—0·5	+0·26	+0·13	−0·15	

* The structure of these substituents is relatively complex (Koch, *J.*, 1949, 408; Koch and Moffitt, *Trans. Faraday Soc.*, 1951, **47**, 7; Barnard, Fabian, and Koch, *J.*, 1949, 2442) but their mesomeric effect seems to be of no importance here and they are included in Table 1.

TABLE 2. *Class b.*

Substituent	NR_2	OR	Cl, Br, I
σ_m	−0·25	+0·1	+0·35
σ_p	−0·6	−0·3	+0·25

Within the limits of accuracy of the perturbation treatment, then, both the σ_m and the σ_p constants of the class (a) substituents originate in the inductive effect of these groups. This effect is usually [3] represented as :

$$\sigma_r = \gamma(q_r - 1) = \delta\alpha_a \cdot \gamma \cdot \sum_s \pi_{rs} \cdot \varepsilon^n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where γ is a proportionality constant between the σ-constant and charge (q_r), carbon atom a of the benzene ring carries the substituent, $\delta\alpha_a$ is the change in the coulomb integral of this carbon atom resulting from the introduction of the substituent, π_{rs} is the mutual atom polarisability of atoms r and s, n is the number of bonds between atoms a and s, and ε is a constant. A relation between σ_m and σ_p is required in order to derive a value of ε and hence of the $\delta\alpha$-values of the substituents. Such a relation is apparent from Tables 1 and 2, namely, that the σ_m- and σ_p-constants are equal to within the precision of the Hammett equation itself, for substituents of class (a). There is no significant drift in either direction, and this equality does not hold for substituents of class (b).

Combination of this equality with equation (1) and the π_{rs} values [16] ($\pi_{11} = +43/108$, $\pi_{12} = -17/108$, $\pi_{13} = +1/108$, $\pi_{14} = -11/108$) gives a cubic in ε :

$$\varepsilon^3 - 0{\cdot}65\varepsilon^2 + 0{\cdot}25\varepsilon - 0{\cdot}1 = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

(terms in ε^4 and higher powers have been neglected in the expansion of equation 1). Equation (2) has one real root at +0·53. This value of ε is rather higher than that (0·33)

* Attached to the benzene ring by the central, not by the terminal atom.

† The absence of a mesomeric effect in the *para*-position to the CN and CO groups follows [11] from the fact that their parent hydrocarbon is an even alternant—styrene—and, in both benzene and styrene, the charge at the *para*-position is unity. The NO_2 and CO_2R groups have as their parent hydrocarbon the 2-phenylallyl carbanion and here the non-bonding molecular orbital is confined to the terminal atoms of the allyl portion of the molecule. The charge at the *para*-position of the benzene ring is thus unity both in the substituted and in the unsubstituted molecules and the mesomeric effect vanishes.

[13] Pullman and Pullman, "Les Theories Electroniques de la Chimie Organique," Masson et Cie, Paris, 1952, chapter 10.

[14] Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 265.

[15] Bordwell and Boutan, *J. Amer. Chem. Soc.*, 1956, **78**, 87.

[16] Wheland and Pauling, *ibid.*, 1935, **57**, 2086.

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used by Jaffe [1] but is in line with that suggested by Branch and Calvin [17] and by Dewar,[18] *i.e.*, 0·4—0·5. The earlier value of 0·1, derived by Wheland and Pauling [16] from a perturbation treatment of electrophilic substitution in pyridine, seems much too small.

In order to obtain values for the $\delta\alpha$'s in terms of β,* the proportionality constant γ must be considered. Jaffe's value [2] of γ (−15·5) is based on a value of 0·33 for ε and it is not clear how the former should be modified now that ε is taken as 0·53. Rather than report the $\delta\alpha$'s as ratios, the value of −15·5 has been used for γ but the numerical magnitude of the results must be accepted with reservation. The point is not of great importance since the ratios of the $\delta\alpha$'s, which are independent of γ, are our primary concern. Hence

$$\delta\alpha_a = 1{\cdot}0\sigma_m = 1{\cdot}0\sigma_p \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

for class (a) substituents and the values of α are numerically equal, when expressed in units of β, to the σ-constants. Average values of the $\delta\alpha$'s are reported in Table 3, together with Branch and Calvin's I values.[17] The latter are discussed below. Values [19] for the SMe

TABLE 3.

Substituent	NR_3^+	SR_2^+	NO_2	CN	SO_2Me	SOMe	CF_3	COR	CO_2R	CO_2^-	Alkyl
$\delta\alpha_a$	+0·9	+1·0	+0·75	+0·7	+0·65	+0·55	+0·45	+0·3—0·4	+0·45	+0·1	−0·1
I	+13·6	+15·7	+12·1	+10	—	—	—	+5	+6·5	−1·9	—

group fit the generalisation less well ($\sigma_m = +0{\cdot}15$, $\sigma_p = 0{\cdot}0$), but here, as with the alkyl group, the inductive effect is not large and small mesomeric effects, not revealed by the perturbation treatment, may be of comparable importance.

The order of inductive constants ($\delta\alpha$'s) given in Table 3 agrees well with general expectation. The positively charged trialkylammonium and dialkylsulphonium ions have the largest inductive constants of all groups, while the nitro- and the cyano-group have the largest constants of the uncharged groups. At the opposite extreme, the alkyl group is alone in having a small electron-repelling effect, while the negative charge of the carboxy-anion is sufficient to reduce the electron-attracting effect of the alkoxycarbonyl group markedly. The sulphone and sulphoxide groups are interesting, the second oxygen atom increasing the electron-attracting power of the group by 0·1β.

The monatomic substituents remain for discussion. Although they exhibit a mesomeric effect in the *para*-position, the *meta*-position is not affected mesomerically, so that the inductive constants of the groups may be obtained from the σ_m-values as before. The results are presented in Table 4. The $\delta\alpha$ values are not in agreement with general expectation. The latter is derived from the belief that the coulomb integral is closely related to

TABLE 4.

Substituent	NR_2	OR	Cl, Br, I
$\delta\alpha_a$ (= σ_m)	−0·25	+0·1	+0·35
($\sigma_p - \sigma_m$)	−0·35	−0·4	−0·1

the electronegativity of the heteroatoms. Unfortunately, difficulties related to the nature of the Hückel Hamiltonian prevent a precise description of the coulomb integral and it is becoming increasingly clear that this simple relation is inadequate. Bassett, Penfold, and Brown [20] recently suggested that the position of the heteroatom in the mesomeric system is of greater importance than has hitherto been realised: an example will clarify the point. Consider the nitrogen atoms in pyridine and in aniline. The isoelectronic hydrocarbons are benzene and the benzyl anion. When one of the benzene carbon atoms is replaced by

* β is the standard carbon–carbon bond resonance integral. Overlap is neglected.

[17] Branch and Calvin, "The Theory of Organic Chemistry," New York, Prentice-Hall, 1941, chapter 6.
[18] Dewar, *J.*, 1950, 2329.
[19] Bordwell and Cooper, *J. Amer. Chem. Soc.*, 1952, **74**, 1058.
[20] Bassett, Penfold, and Brown, *Chem. and Ind.*, 1956, 892.

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the nitrogen atom to form pyridine, the nitrogen atom is taking over a place of unit charge, while, when the nitrogen atom replaces the carbon atom of the methylene group of the benzyl anion to form aniline, it is taking over a place carrying a large fraction of a unit of negative charge in excess of that on the carbon atom of benzene. The overall result is that the nitrogen atom of aniline, instead of being weakly electron-attracting as is the nitrogen atom of pyridine, becomes weakly electron-repelling. Jaffe [1] reached the same conclusion. The more strongly electron-attracting oxygen atom is effectively neutralised by this positional effect, and the strongly electron-attracting halogens are reduced until they are weakly electron-attracting. The difference between the σ_p- and σ_m-constants of the monatomic substituents (Table 4) should then represent the mesomeric effect at the *para*-position of these substituents. It is unlikely that much significance is to be attached to the magnitude of these $(\sigma_p - \sigma_m)$ factors, but it is encouraging that they are of the correct sign and in a reasonable order, the nitrogen and oxygen atoms conjugating with the ring more strongly than the halogen atoms.

Branch and Calvin [17] developed a similar series of inductive constants (I) from acid strengths. Their I values are reproduced in Table 3 and there is good agreement in both order and relative magnitude with the present series.

The inductive constants developed in this paper go some way towards putting the qualitative ideas of the resonance theory on a quantitative basis. Some instances of the utility of the series have come to the author's notice. In particular, the high inductive constants of the nitro- and the cyano-group suggest the explanation of some observations in the literature. Sixma [4] found that a treatment of σ-constants, which proved satisfactory for all other substituents, failed with these groups and he attributed this to their large inductive effects. In a molecular-orbital investigation of the directive effects of substituents on the phenyl radical addition to, or substitution in, the substituted benzene ring,[21] a reaction which is entirely governed by the mesomeric effects of most substituents, the two substituents which deviate from the calculations are the nitro- and the cyano-group. Evidently their inductive effects are sufficiently large to be comparable with their mesomeric effects.

Another situation in which the large inductive constants of these groups are evident is the pyrolysis of substituted benzyl bromides reported by Leight, Sehon, and Szwarc.[22]

TABLE 5.

Substituent	Me			Cl			NO_2		CN	
Position	*o*	*m*	*p*	*o*	*m*	*p*	*m*	*p*	*m*	*p*
$-\delta D$ (kcal./mole)	2·0	0	1·4	0·9	0·1	0·4	2·1	1·1	1·4	0·7

The bottom row of Table 5 indicates the decrease in activation energy ($-\delta D$) resulting from the introduction of the substituents into the benzene ring in the reaction, $Ph{\cdot}CH_2Br \longrightarrow Ph{\cdot}CH_2{\cdot} + Br{\cdot}$. With methyl and chloro-substituents, the familiar mesomeric effects of these groups are evident; the *ortho*-substituent is the strongest activator, the *para*-substituent is less activating, and the *meta*-substituent has little or no effect on the reaction rate. Nitro- and cyano-groups exhibit a different behaviour and it seems that their inductive effects are large enough to compete with their mesomeric effects.

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[*Received, January 30th*, 1957.]

[21] Peters, unpublished work.
[22] Szwarc, Leigh, and Sehon, *J. Chem. Phys.*, 1951, **19**, 657; Leigh, Sehon, and Szwarc, *Proc. Roy. Soc.*, 1951, *A*, **209**, 97.

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516. *Physicochemical Studies on Starches. Part V.* The Effect of Acid on Potato Starch Granules.*

By J. M. G. Cowie and C. T. Greenwood.

The degradative effect of 0·2M-hydrochloric acid at 45° on the granular structure and molecular size of the components of two varieties of potato starch has been examined. The fractionated starch components were characterised by iodine-binding power, osmotic pressure, viscosity, and sedimentation. The mode of acid attack was similar for both samples. Under the conditions used, the granular structure was apparently unchanged, but both the amylose and the amylopectin component were degraded. The rates of degradation indicated that the amylopectin underwent preferential hydrolysis. The implications of these results with regard to granular structure are discussed.

Notwithstanding the large amount of work carried out on starch, little is yet known of the fine structure of the granule and the manner in which amylose and amylopectin are incorporated into it. It has been suggested that amylose is found in the granule preferentially at the centre, but it has also been maintained that it is evenly distributed throughout.[1] One approach to this problem is to study the effect of acid-treatment on the granule by estimating, after fractionation, the molecular size of the components. If the granule has an outer layer of amylopectin, the latter should be preferentially hydrolysed, whereas if there is uniform distribution both components should be degraded. In studies of the granular structure of potato starch, we have therefore examined such effects. Previous investigations along these lines have had contradictory results: Meyer and Menzi [2] reported that acid-treatment of potato and maize starch gives simultaneous degradation of both components, whilst Kerr [3] reported preferential degradation of amylopectin in maize starch. However, Meyer and Menzi [2] measured molecular weights by the dinitrosalicylic acid method, which has been shown to be unreliable for absolute molecular weights,[1] and Kerr [3] evaluated his osmotic data for amylopectin solutions by a method which has not yet been substantiated.[1] The studies reported here were undertaken in an effort to clarify the position, as all physical properties of the granule depend ultimately on granular structure and any method of tackling the latter problem is thus important.

Experimental Methods

Isolation and Purification of Potato Starch.—Potatoes (var. Redskin and Arran Banner severally) were thickly peeled, sliced, and then minced into ethanol to inhibit enzymic activity. After extraction with ethanol for 2 min. in an " Atomix " blendor, the pulp was filtered through muslin, and the filtrate *immediately* centrifuged. The supernatant liquid was discarded, and the starch washed by repeated sedimentation in 0·1M-sodium chloride. The residual pulp was then re-extracted 3—4 times with saline in the blendor. (Although extraction was obviously incomplete, the residual pulp was then discarded.) Starch rapidly sedimented from the filtrates. The starch-products were combined, suspended in 0·1M-sodium chloride, and shaken with toluene ($\frac{1}{10}$ vol.) overnight to denature protein.[4] After the granules had been allowed to sediment, the coagulated protein–toluene layer was discarded, and the extraction repeated four times to yield pure starch, which was stored in 0·1M-sodium chloride under toluene at 0° (Arran Banner) or washed free from salt and stored under methanol at 0° (Redskin) (Found, for both samples: N, 0·02%).

Characterisation of Starch Products.—The efficiency of fractionation and the overall effect of acid-treatment on the granules was followed by measuring the amount of iodine bound by

* Part IV, *J. Polymer Sci.*, 1957, in the press.

[1] For a review see Greenwood, *Adv. Carbohydrate Chem.*, 1956, **11**, 335.
[2] Meyer and Menzi, *Helv. Chim. Acta*, 1953, **36**, 702.
[3] Kerr, *Stärke*, 1952, **4**, 39.
[4] Greenwood and Robertson, *J.*, 1954, 3769.

the various starch products. In view of the insensitivity of optical-absorption methods, the binding power was measured in the semimicro differential-titration apparatus previously described.[5] Titration conditions were: [iodide], 0·01M; pH, 5·85; temp., 20°.

The total free iodine in the starch solution was plotted against the mg. of iodine bound per 100 mg. of starch, and estimations of iodine affinity (the preferential uptake of iodine by the linear amylose component) were made by extrapolating the linear portion of the titration curves to zero free-iodine concentration. Calculations of the approximate percentage of amylose were made from the observed iodine affinity on the assumption that pure potato amylose bound 19·5% of iodine under these conditions.

Treatment of Granules with Acid.—Potato starch (10 g.; var. Redskin, washed free from salt) was stirred slowly (20 revs./min.) in 0·2M-hydrochloric acid (500 ml.) at 45° under oxygen-free nitrogen. Portions (125 ml.) were removed after 1, 2, 3, and 4 hr. severally (Expt. I). The starch was immediately washed 8—12 times with distilled water in the centrifuge until free from acid and then shaken with methanol for 24 hr. The samples were stored under methanol.

The above was repeated (Expt. II), except that starch samples (var. Arran Banner) were removed at intervals of ½, 1, 2, 3, 4, and 24 hr.

Estimation of Amount of Granule Solubilised by Acid.—A 2% suspension of starch in 0·2M-hydrochloric acid was kept at 45° for 1 hr. under nitrogen. A portion of the suspension was removed, centrifuged, and reduced in volume, and the amount of glucose obtained on hydrolysis by 3N-sulphuric acid for 2 hr. at 100° was estimated by the alkaline ferricyanide–ceric sulphate method of Lampitt, Fuller, and Coton.[6] The starch was re-treated with acid for 3 hr., and the additional glucose found in the supernatant liquors estimated. The residual starch granules were weighed.

To investigate whether oligosaccharides were present inside the granule after acid-treatment, starch (2 g.; treated with 0·2M-hydrochloric acid for 4 hr.) was gelatinised at 70° in water (400 ml.) for 1 hr. under nitrogen, and amylose precipitated with butan-1-ol. The supernatant liquors were then reduced to dryness, extracted with 50% methanol, and examined chromatographically (solvent: butan-1-ol–benzene–pyridine–water: 5 : 1 : 3 : 3; top layer; development time, 72 hr. at 18°).

Fractionation of Acid-treated Starches.—A slurry of starch in methanol was carefully added to vigorously stirred boiling water (500 ml.) under nitrogen, and boiling continued for 1½ hr. (Expt. I). (In Expt. II, the boiling was continued for 1 hr.) The solution was then allowed to cool to 60°, powdered thymol (0·5 g.) added, and the mixture set aside at room temperature (18°) for 3 days before the amylose–thymol complex was removed on the Sharples super-centrifuge. The amyloses were then purified by recrystallisation twice (Expt. I) from hot butan-1-ol saturated water, and were stored as the butan-1-ol complexes. Only one recrystallisation was carried out in Expt. II. Solid amyloses were isolated by stirring the butanol complex several times with butan-1-ol and then drying it *in vacuo* at 75°.

The amylopectin-containing supernatant liquors from the thymol–precipitates were freeze-dried directly, refluxed with methanol to remove thymol (3 times; 1½ hr. each), redispersed in water, and freeze-dried. In Expt. II, the supernatant liquors were extracted twice with ether before freeze-drying. This procedure yielded more soluble products.

Fractionation of Original Starch.—A 0·5% solution of starch was dispersed as above (1½ hr. for Expt. I and 1 hr. for Expt. II). After formation of the thymol complex, the amylose was reprecipitated three times with butan-1-ol and stored as this complex. Amylopectin was obtained as above.

Acetylation of Amyloses.—A portion of the butanol complexes of each of the amyloses from Expt. I was acetylated under conditions of minimum degradation[4] with pyridine and acetic anhydride at room temperature.

Estimation of Length of Unit Chain for Amylopectins.—The amylopectins from Expt. II were oxidised with sodium metaperiodate at 2° by Potter and Hassid's method[7] with the modification[8] that the liberated formic acid was estimated by titration to pH 6·25. The yield of formic acid was constant after 25 hr.

[5] Anderson and Greenwood, *J.*, 1955, 3016.
[6] Lampitt, Fuller, and Coton, *J. Sci. Food Agric.*, 1955, **6**, 656.
[7] Potter and Hassid, *J. Amer. Chem. Soc.*, 1948, **70**, 3488.
[8] Anderson, Greenwood, and Hirst, *J.*, 1955, 225.

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Measurements of Limiting Viscosity Number.—The specific viscosity ($\eta_{sp.}$) of the polysaccharide solutions was determined at several concentrations at 22·5°, and the limiting viscosity number $[\eta]$ determined graphically from the relation $[\eta] = \lim_{c \to 0}(\eta_{sp.}/c)$. Concentrations were expressed [9] as g./ml. Measurements were made on both of the unsubstituted components in M-potassium hydroxide, and on the acetylated amyloses in chloroform solution. Techniques were as previously described.[4]

Solution and concentration estimation was as follows:

(a) *For amyloses.* A portion of well-centrifuged butanol complex was dissolved directly in M-potassium hydroxide. Concentrations were then determined by hydrolysing a portion of the diluted resultant solution, and determining the reducing power as above.[6] The method was calibrated by standard solutions of glucose. Preliminary experiments indicated a recovery of 98—102% of glucose for hydrolysed "AnalaR" soluble starch. {Control experiments showed that the limiting viscosity number for a given sample was the same within experimental error whether solution had been achieved *via* the butanol complex or directly from the dried solid. However, the value of Huggins's constant (k') in the relation

$$\eta_{sp.}/c = [\eta] + k'[\eta]^2 c$$

varied.}

(b) *For amylopectins.* Solutions were prepared by weight.

(c) *For amylose acetates.* Concentrations were determined after measurements as before.[4]

Measurements of Osmotic Pressure (with W. N. Broatch).—Osmotic pressures (π) of the amylose acetates in chloroform solution were determined at 22·5° in the instrument previously described.[10] The membrane used was of No 600 gel-Cellophane, which had been dehydrated by acetone and then conditioned to solvent. The cell constant, for a 0·04 cm. diameter capillary,[11] was independent of the meniscus level, and was reproducible within the setting of the cathetometer (±0·001 cm.). Any deviation from the cell constant which developed after use was thought to be due to contamination of the solution capillaries by evaporated polymer films (particularly with solutions of high viscosity) *although evaporation in this instrument is reduced.* The resultant polymer film is insoluble even after repeated washings of the solution chamber with solvent. Variations in cell constant were not therefore due to (*a*) solute adsorption on the membrane or (*b*) membrane dissymmetry effects. These "effects" observed previously [12] might be similarly explained. Although such variations of cell constant were avoided by working at a different level in the solution capillary, it was considered more satisfactory to dismantle and clean the apparatus.

Concentrations were estimated in duplicate after determination. The procedure adopted was to fill the osmometer with the most concentrated solution, determine the osmotic pressure, remove two volumes (by weight) for estimation of concentration, and add an equivalent volume of solvent. The solution was then carefully mixed, and the osmotic pressure of the diluted solution determined. Pressures were measured statically after an initial setting to 1·0 cm. below the expected value. There was no evidence of solute permeation of the membrane. In each experiment, the value of the intercept $(\pi/c)_0$ was obtained from the linear graph of π/c *versus* c, where π was expressed as dynes g.$^{-1}$ cm., and c as g. cm.$^{-3}$. Number average molecular weights ($\bar{M}_n$) were then calculated from van't Hoff's equation $\bar{M}_n = \boldsymbol{R}T(c/\pi)_0$.

Sedimentation Measurements.—Determinations were made with an electrically driven Spinco ultracentrifuge on both components dissolved in 0·2M-potassium hydroxide. Detailed results will be presented elsewhere.

Results

Examination of Acid-treated Whole Starches.—Microscopic examination showed that the granules which had been treated with acid for 4 hr. appeared unchanged and were still birefringent. However, the granules dispersed more readily to form a less viscous paste. The granules which had been subjected to 24 hr. treatment behaved similarly, although some split granules were visible.

Estimations of the amount of glucose in the acid supernatant liquors showed that after 1 hr. 0·2% and, after a further 3 hr., 0·8% of the granule was solubilised. Hence only about 1% of

[9] I.U.P.A.C. nomenclature, *J. Polymer Sci.*, 1952, **8**, 257.
[10] Gilbert, Greenwood, and Graff-Baker, *ibid.*, 1951, **6**, 585.
[11] Broatch and Greenwood, *ibid.*, 1954, **14**, 593.
[12] Cf. Masson and Melville, *ibid.*, 1949, **4**, 323.

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the total weight of the granules was solubilised as glucosans or reducing sugars in the 4 hr. treatment. Chromatographic examination of the gelatinised granules indicated that at the most only traces of oligosaccharides (probably tri- or tetra-glucosans) could have been present after acid-treatment.

An estimate of the apparent reducing power was obtained by titrating the starches directly with the alkaline ferricyanide reagent. The results indicated that the reducing power increased regularly with time of acid-treatment as shown :

Time of acid-treatment (hr.)		0	1	2	3	4
No. ml. of M/100-ceric sulphate required/1 g. of starch	In N_2	0·40	2·80	5·00	7·40	9·83
	In O_2	0·10	4·90	8·75	13·92	18·40

An experiment in the presence of oxygen indicated an apparent greater increase in reducing power.

FIG. 1. *(a) Typical iodine-titration curves for acid-treated starches. The original potato starch is shown as the dotted curve. The numbers on each curve are the times of acid-treatment of the starch (in hr.). (b) Typical iodine-titration curves for acid-treated amylopectins. Potato amylopectin (containing 0·5% of amylose) is shown as the broken curve. Curves 1 and 2 are for amylopectins isolated after 3 and 4 hours' treatment, respectively.*

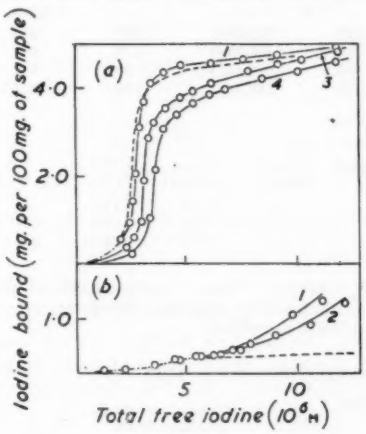
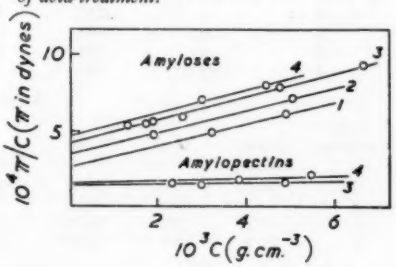


FIG. 2. *Graph of π/c versus c for the acetylated starch components in chloroform solution. The numbers on the curves represent the hours of acid-treatment.*



Potentiometric iodine-titration curves showed changes in iodine affinity of the samples: there was an apparent increase up to about 1 hr. followed by a decrease thereafter (Fig. 1*a* shows typical titration curves). In addition, the slope of the linear portion of the curve increased with time of acid-treatment, as did the activity of free iodine necessary to saturate the linear amylose component.

Time of acid-treatment (hr.)		0	½	1	2	3	4
Redskin starch	Iodine affinity	4·03	—	4·25	—	3·89	3·10
	Amylose (%)	20·70	—	21·80	—	20·00	15·90
Arran Banner starch	Iodine affinity	4·03	4·51	4·30	4·11	3·60	3·07
	Amylose (%)	20·70	23·10	22·00	21·10	18·50	15·80

Properties of the Fractionated Components.—Potentiometric titration showed a normal curve (cf. ref. 4) for the amylose components, whilst the amylopectin curves were abnormal (Fig. 1*b*) and did not show the linear increase in bound iodine previously observed.[5] Fig. 2 shows the results of osmotic-pressure determination for the acetates from Expt. I. The properties of the separated fractions from both experiments are shown in Tables 1 and 2.

The results of physical measurements carried out on solutions of both components in alkali were reproducible, and the solutions were stable for the time required for measurement. The

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sedimentation measurements confirmed that depolymerisation effects, particularly in the case of the amylopectin components, were real.

Rates of Degradation.—Degradation of the components was expressed as (1) the number of bonds broken per initial polysaccharide molecule, and (2) the variation of $1/[\eta]$, both as a function of time. The use of the latter function instead of $[\eta]$ directly is justified as follows :

The number of bonds broken per w g. polysaccharide, $(q) = \frac{Nw}{M_0}\left(\frac{M_0}{M_t} - 1\right)$ where M_0, M_t are the number-average molecular weights at times 0 and t, respectively and N is Avogadro's number. This can be rewritten as

$$q = Nw(1/M_t - 1/M_0)$$

$$\text{or} \quad q \propto \frac{1}{M} \propto \frac{1}{[\eta]} \text{ since in this instance } M = K[\eta].$$

Hence the rate of change of $[\eta]$ with time is *not a direct measure of degradation*, in agreement with McBurney.[14]

The graphs of (bonds broken) *versus* t, and of $[\eta]^{-1}$ *versus* t for the two series of amyloses are

TABLE 1. *Properties of the amylose components.*

Redskin amylose

Acid-treatment (hr.)	Iodine affinity	$[\eta]$ in M-KOH	Calc. $\overline{D.P.}$ [a]	$[\eta]$ of acetate [b]	M. wt. from π	Obs. $\overline{D.P.}$ [c]	$10^{13}S_0$ [d]
0	19·5	470	3480	—	—	—	12·0
1	—	220	1630	370	470,000	1630	9·9
2	20·3	190	1370	335	400,000	1390	8·3
3	—	140	1040	305	302,000	1050	7·3
4	20·7	130	925	270	286,000	990	6·2

Arran Banner amylose

Acid-treatment (hr.)	Iodine affinity	$[\eta]$ in M-KOH	Calc. $\overline{D.P.}$ [a]	$10^{13}S$ [e]	Acid-treatment (hr.)	Iodine affinity	$[\eta]$ in M-KOH	Calc. $\overline{D.P.}$ [a]	$10^{13}S$ [e]
0	19·5	520	3850	13·0	3	—	177	1310	—
½	—	280	2070	—	4	—	152	1130	4·8
1	19·3	225	1670	7·1	24	—	73	540	2·9
2	19·8	201	1490	5·8					

[a] Calc.[13] from $\overline{D.P.} = 7{\cdot}4[\eta]$. [b] Measured in $CHCl_3$ solution. [c] Calc. from previous column. [d] Sedimentation constant in c.g.s. units at infinite dilution obtained by graphical extrapolation from $S = f(c)$. [e] Sedimentation constant in c.g.s. units at $c = 0{\cdot}075$ g./100 ml.

TABLE 2. *The properties of the amylopectin components.*

Redskin amylopectin.

Acid-treatment (hr.)	$[\eta]$ in M-KOH	$[\eta]$ of acetate [a]	M. wt. from π	Obs. $\overline{D.P.}$ [b]	β-Amylolysis limit [c]	$10^{13}S_0$
0	182	—	—	—	56·5	175
1	123	220	—	—	57·4	60
2	118	205	—	—	58·2	52
3	113	220	$1{\cdot}1 \times 10^6$	3800	58·1	43
4	105	200	$1{\cdot}0 \times 10^6$	3500	57·5	35

Arran Banner amylopectin.

Acid-treatment (hr.)	$[\eta]$ in M-KOH	Av. length of unit chain	$10^{13}S_0$ [d]	Acid treatment (hr.)	$[\eta]$ in M-KOH	Av. length of unit chain	$10^{13}S_0$ [d]
0	182	25	175	3	108	24	42
½	112	24	63	4	106	24	34
1	122	26	58	24	48	22	14
2	110	25	49				

[a] Measured in $CHCl_3$ solution. [b] Calc. from previous column. [c] Results obtained through the courtesy of Mr. I. D. Fleming and Dr. D. J. Manners. [d] Sedimentation constant in c.g.s. units at infinite dilution obtained by graphical extrapolation from $S = f(c)$.

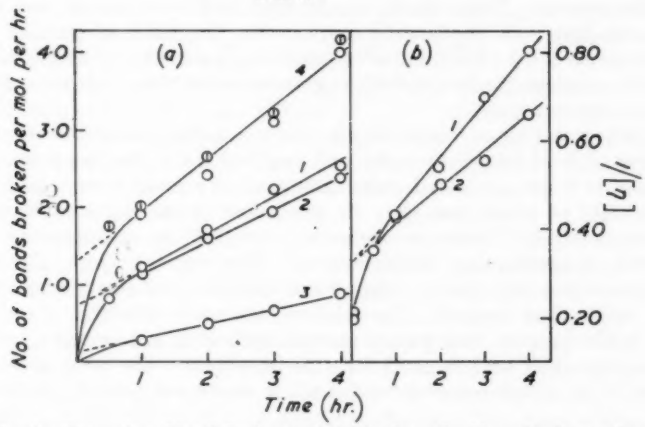
[13] Cowie and Greenwood, unpublished results.

[14] McBurney in Ott and Spurlin's "Cellulose and Cellulose Derivatives," Interscience, New York, 1954, 2nd edn., Vol. I, p. 99.

shown in Fig. 3. It is of interest that in neither instance do the linear portions of the curves extrapolate to the origin. In Fig. 3*a*, the linear portions of the curves correspond to rates of 0·5 and 0·4 (expressed as the number of bonds broken per initial amylose molecule per hr.) for the Redskin and Arran Banner amyloses, respectively. A linear relation (curve 3, Fig. 3*a*) was also found for $(S_0/S_t - 1)$ *versus* t, where S_0, S_t are the sedimentation constants at times 0 and t respectively. The rate of degradation from this curve (0·2) was less than the absolute rate because the diffusion constant for the linear amylose molecule must change considerably with decrease in $\overline{\text{D.P.}}$, and hence changes in S were not directly proportional to changes in $\overline{\text{D.P.}}$

For amylopectins, the degradation could not be calculated unambiguously in view of the difficulty in obtaining absolute values for the molecular weight. However, again it was found that the graph of $(S_0/S_t - 1)$ *versus* t was linear, and on the assumption that for this component

FIG. 3.



(*a*) *Graph showing the number of bonds broken per initial polysaccharide molecule as a function of time.*
(1) *Redskin amylose.* (2) *Arran Banner amylose.* (3) $(S_0/S - 1)$ *for Redskin amylose.*
(4) $(S_0/S - 1)$ *for Redskin* (○) *and Arran Banner* (ⓘ) *amylopectins, respectively.*

(*b*) *Graph of* $1/[\eta]$ versus t *for the amylose components.*
(1) *Redskin amylose.* (2) *Arran Banner amylose.*

the diffusion constant was unlikely to vary considerably, the linear portion of this curve corresponded to a rate of 0·7 (units as above). This is likely to be a minimum rate as any disproportionate increase in the diffusion constant with time of degradation will increase the slope. Again the extrapolated linear portion of this curve did not pass through the origin.

DISCUSSION

Experimental conditions were chosen such that our results are strictly comparable with those of both Meyer and Menzi [2] and of Kerr.[3] However, these authors presented insufficient data to permit comparison of actual *rates* of degradation of the two components. (Kerr's data unfortunately could not be replotted since " fluidities " were reported rather than times of acid-treatment.) At best, only general comparisons are possible.

The starches from the two varieties of potato (Redskin and Arran Banner) gave similar results, and hence can be considered to behave identically.

General Properties of Acid-modified Granules.—The action of acid does not alter the birefringent properties of the granule. There was no evidence of swelling in the acid media. It therefore appears that acid-treatment has preferentially affected the *amorphous* rather than the crystalline region of the granule. Sjoström [15] and Meyer and Bernfeld [16] observed similar effects, and Alsberg [17] also reported the treatment with hydrochloric

[15] Sjoström, *Ind. Eng. Chem.*, 1936, **28**, 63.
[16] Meyer and Bernfeld, *Helv. Chim. Acta*, 1940, **23**, 890.
[17] Alsberg, *Plant Physiol.*, 1938, **13**, 295.

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acid (7·5%) destroyed the ability of the granule to swell and suggested that the portion responsible for swelling had been modified.

It was thought that estimation of the amount of reducing sugar produced in the acid supernatant liquor was the only suitable method for determining any loss in weight of the granule on acid-treatment. Only 1% was found after 4 hr. The possibility that oligosaccharides might have been produced and that these were unable to diffuse out readily from the persistent granular structure and so account for (1) the abnormal iodine titration curves for the whole starches and the amylopectins, and (2) the β-amylolysis results (particularly as the amylopectins were freeze-dried directly) was shown to be incorrect.

Potentiometric titrations indicated changes in the apparent percentage of linear material in the granule. These results can be explained by assuming that the material dissolving in the first hour is primarily amylopectin (the 0·2% of granular weight lost accounting for a rise of 0·3—0·5% in the effective amylose-content), whilst that dissolving later is primarily amylose (the further 0·8% of granular weight lost being equivalent to about 4% of total amylose content).

Although Meyer and Menzi [2] reported no change in iodine-binding power of their acid-treated starches, it is of interest that the acid-modified maize starches studied by Schoch and his colleagues [18] also possessed iodine affinities very much lower than the original. The iodine affinity of starch can only be unaffected if the degradation products are solubilised completely (and there is no evidence for this), or acid-modified components have unaltered iodine-binding characteristics. However, although the fractionated amyloses possessed the usual iodine binding characteristics, all the amylopectin fractions bound more iodine than normal. The relative constancy of length of unit chain and β-amylolysis limits suggests that purely random hydrolytic action must have occurred, and no explanation can be advanced for this behaviour. The increased slope of the linear portion of the titration curves for the whole starches is probably accounted for on this basis.

The method of isolation of the amylose involved reprecipitations as the butan-1-ol complex which might involve the loss of some short chains. This was decreased in the case of Arran Banner samples by carrying out only one recrystallisation, although in neither experiment was there any apparent loss in amylose at this stage.

Degradation of the Components in the Granule.—The curves of rates of degradation (Fig. 3*a*) show that amylopectin is degraded considerably faster than amylose. Since the former must be a minimum rate, and also since the α-1 : 6-bonds (present to the extent of about 1 in 20) are reported [1] to be stronger than α-1 : 4-bonds, amylopectin must be preferentially degraded and is therefore far more accessible to attack than the amylose. The curves for both components do not extrapolate to zero time, which indicates (by comparison with cellulose chemistry) that acid-modification of the granule takes place in two stages, a rapid attack on amorphous regions, followed by a slower attack on more crystalline areas. This occurs for both components, but the results indicate a larger preferential scission of amylopectin rather than of amylose initially. (Although this two-stage process might well indicate the preferential scission of anomalous linkages, it is thought that in experiments involving whole starch granules such interpretations have to be made with caution.)

The results show that, even after 24 hr., degradation of amylose in the granule is relatively limited (to about 6 bonds per initial molecule). This contrasts markedly with the behaviour of the isolated amylose under similar conditions (preliminary unpublished experiments having indicated that such degradation is much more rapid), and suggests in contradiction to Lathe and Ruthven's conclusions [19] that penetration into the inner region of the *unswollen* granule is time-dependent and not instantaneous. Any *initial*

[18] Lansky, Kooi, and Schoch, *J. Amer. Chem. Soc.*, 1949, **71**, 4066.
[19] Lathe and Ruthven, *Biochem. J.*, 1956, **62**, 665.

attack will therefore occur preferentially in the surface layer of the granule before hydrogen ions diffuse into the inner regions.

The different rate curves for the two amylose fractions could be due to the prior storage of Redskin starch in methanol with subsequent dehydration and " splitting " of the granular structure permitting more ready access of reagent. This effect is not thought to be significant in these experiments.

Our degradation results appear to support Kerr's conclusions [3] that amylopectin is preferentially degraded. Ulmann [20] has reached a similar conclusion from chromatographic evidence. In view of the relatively small changes in the number of bonds broken, the changes in reducing power observed by Meyer and Menzi [2] can probably be explained by the " peeling action " [21] of their reagent.

Granular Structure.—Little is yet definitely known,[1] although crystallinity is evident in all starch granules (including those of the waxy variety). The formation of " crystallites " by the alignment of the long unbranched amylose molecules is very likely, but in potato starch granules amylose accounts for only 20% of the structure. The question of the compacting of the remaining 80% is far more difficult, even to account for the reported *total* 50—60% crystallinity of the granule.[22] In particular, it is difficult to see how amylopectin molecules can pack themselves to any degree of crystallinity if they have the three-dimensional structure envisaged by Meyer. As suggested by Greenwood,[1] a two-dimensional structure might be more likely. Much depends on the actual shape of the amylopectin molecule, and experiments are in progress to determine this.

Unless amylose exists preferentially at the surface (no evidence exists for this), the surface layer of the granule must be predominantly amylopectin by virtue of its amount. (Evidence for the existence of a true amylopectin outer layer is contradictory, but unpublished experiments have indicated that such a layer may exist.) The amylopectin is most likely to form the amorphous regions of the granule, although, as Meyer has suggested, the outer branches of several amylopectin molecules might well align themselves to form a small crystallite. In addition, the outer branches might well link up with amylose in the crystalline regions, and amylose (particularly the short-chain material) might well form part of the amorphous region. Swelling of the granule would be associated with the amorphous branched component.

This concept of granular structure is consistent with the effects observed on acid-treatment. The primary attack of acid on the potato granule is on the surface membrane, because of the very limited swelling at the temperature of the experiment. The more freely accessible outer chains of the surface amylopectin molecules might well be degraded sufficiently to dissolve completely. This occurs mainly in the first hour, and is accompanied by a simultaneous attack on amylose and amylopectin in the amorphous regions. Degradation of the components arises by diffusion of the acid into the granule in the absence of swelling, and degradation takes place throughout the granule, but at a decreased rate in the crystalline regions. The hydrogen bonding responsible for the crystalline structure must be relatively strong by virtue of the limited hydrolytic effects observed even after 24 hours' treatment.

In view of the complex, but ordered, nature of the structure of the granule, it is not surprising that the mode of action of the acid is complex. Further methods of studying granular structure are being examined.

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Department of Chemistry, University of Edinburgh. [*Received, February 6th*, 1957.]

[20] Ulmann, *Makromol. Chem.*, 1956, **20**, 143.
[21] Bottle and Gilbert, *Chem. and Ind.*, 1954, 1201.
[22] Rundle, Daasch, and French, *J. Amer. Chem. Soc.*, 1944, **66**, 130.

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517. *The Water-soluble Polysaccharides of* Cladophora rupestris.*

By I. S. Fisher and Elizabeth Percival.

Water-soluble sulphated polysaccharides containing mainly arabinose, galactose, and xylose and small amounts of rhamnose and glucose have been extracted from *Cladophora rupestris*. Each of the sugars has been isolated as crystals. Chloroform-extraction of the acetylated material separated a small quantity of a glucose-rich fraction resembling laminarin. Methylation studies on the glucose-free residue have revealed a highly branched structure and established the presence of some 1 : 3-linked arabinose, galactose, and rhamnose, and some 1 : 4-linked xylose. Partial hydrolysis and periodate experiments support these results.

The polysaccharide material extracted from the green seaweed, *Cladophora rupestris*, by boiling water or by dilute hydrochloric acid (pH 3—4) had a nitrogen content of 3—4%. Neither ammonium salts nor amino-sugar units could be detected in it, but amino-acids were present in acid hydrolysates. This indicated contamination with protein to the extent of 20—25% and the usual methods for removal of protein were investigated.[1-7] None proved entirely satisfactory but the best and most economical was partial precipitation of the protein with 4% trichloroacetic acid,[8] followed by precipitation of the polysaccharide by addition of ethanol to the clarified, dialysed, concentrated filtrate. Polysaccharide containing 2·0 and 1·8% of nitrogen was precipitated from solutions containing 50 and 70% of ethanol respectively. After removal of these two fractions addition of ethanol to a concentration of about 95% precipitated an off-white powder (A) (N, 1·26%; yield 6·5% from the cleaned dried weed), $[\alpha]_D$ +69°. Examination of the different fractions precipitated from aqueous solution by different concentrations of alcohol showed them to be essentially similar in sugar content and each contained the same amount of sulphate. Although several treatments of material (A) by the Sevag method [9] effected a further slight reduction in nitrogen content (1·26 ⟶ 1·05%) the recovery was very low. Hot N-alkali reduced the nitrogen content of material (A) to 0·06% but caused considerable degradation of the carbohydrate material. Consequently all subsequent investigations were carried out on material (A).

Similar results have been obtained with the sulphated polysaccharide from the green seaweed, *Ulva lactuca*;[10] the original extracts contained 25% of protein and although repeated treatment with chloroform–butanol [9] reduced the nitrogen content to 1·01% the recovery of polysaccharide was very poor.

Paper chromatography of the hydrolysate from material (A) showed the presence of arabinose, galactose, xylose, rhamnose, and glucose in the molar proportions 3·7 : 2·8 : 1·0 : 0·4 : 0·2. Concordant estimations of rhamnose were difficult to obtain, the figure quoted being an average. It should be emphasised that the hydrolysates of all the fractions and products from the different purification procedures contained all these five sugars. Column chromatography of the hydrolysate gave L-rhamnose, α-D-xylose,

* A preliminary account of some of this work was given at the Second International Seaweed Symposium at Trondheim, 1955.

[1] Fugita and Iwatake, *Biochem. Z.*, 1931, **242**, 43; Arni and Percival, *J.*, 1951, 1826.
[2] Percival and Ross, *J.*, 1950, 717.
[3] Engstrøm and Jakus, *Nature*, 1948, **161**, 168.
[4] Hough, Jones, and Wadman, *J.*, 1952, 3393.
[5] Chanda, Hirst, Jones, and Percival, *J.*, 1950, 1289.
[6] Somogyi, *J. Biol. Chem.*, 1945, **160**, 69.
[7] Stumpf, *ibid.*, 1948, **176**, 240.
[8] Kunitz and Northrop, *J. Gen. Physiol.*, 1936, **19**, 991.
[9] Sevag, Lackmann, and Smollens, *J. Biol. Chem.*, 1938, **124**, 425.
[10] Brading, Georg-Plant, and Hardy, *J.*, 1954, 319.

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L-arabinose, D-glucose, and α-L-galactose, all as crystals which, with the exception of glucose, were further characterised as crystalline derivatives. Glucose was characterised by oxidation to gluconic acid by the specific enzyme D-glucose oxidase. D-Glucose,[11] D-xylose,[12] and D-galactose [13] are fairly common constituents of algal polysaccharides, and L-rhamnose has been reported in *Ulva lactuca*,[10] but the only other reported occurrence of arabinose in an algal polysaccharide is that from the blue-green weed, *Anabaena cylindrica* [14] where it is present to the extent of about 6%.

Addition of potassium chloride to an aqueous solution of material (A) failed to yield a "κ"-fraction [15] similar to that given by carrageenin. Extraction of acetylated (A) by chloroform removed all the glucose (4%) as a glucose-rich fraction which was practically sulphate-free. Further, addition of cetyltrimethylammonium bromide [16] to an aqueous solution of material (A) gave a precipitate which was devoid of glucose. Material (A) gave a schlieren electrophoretic diagram with a symmetrical peak, indicating a monodispersed polysaccharide; it appears that the detection of relatively small amounts of contaminating carbohydrate is beyond the scope and sensitivity of this procedure. Electrophoresis on paper indicated a single sulphated polysaccharide.

Sulphate in the polysaccharide is undoubtedly ethereally linked. It is not reduced on prolonged dialysis and, whereas ions such as calcium could be precipitated from solution, no sulphate could be detected until after hydrolysis. The sulphate content, 19·6%, and that calculated from the sulphated ash, 10·0%, agrees with the ratio 2 : 1 characteristic of polysaccharide ethereal sulphates.[13] After allowance of 8% for protein and 4% for unsulphated glucose-rich fraction the sulphate content of glucose-free material corresponds to seven $SO_3Ca_{\frac{1}{2}}$ radicals to every seventeen sugar residues. The sulphate was extremely stable to alkali, even under conditions which degraded the carbohydrate. Methylation with alkali, under conditions not expected to degrade the polysaccharide, gave a methylated material which contained 16·2% of sulphate. From the alkali-stability of these groups it appears [17] that the galactose units carry the sulphate at position 4, but, as far as the authors are aware, no work has been done on pentose sulphates and it is impossible at this stage to assign the sulphate group to any particular carbon atom of the pentose sugar molecules.

It is well known that it is difficult to methylate sulphated polysaccharides; [18] all attempts to prepare a methylated material from the glucose-free acetate with a methoxyl content higher than 25·1% proved unsuccessful. This methylated material was subjected to methanolysis, the glycosides formed were then hydrolysed by aqueous acid, and the resulting sugars analysed on a cellulose column and on paper. A large number of components, some of which chromatographed at closely similar rates, were detected; this made separation and identification of some of the derivatives exceedingly difficult.

The following sugars were separated and identified: 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose, 2 : 3 : 5-tri-*O*-methyl-D-galactose, and 2-*O*-methyl-D-galactose by chromatography, rotation, methoxyl content, and demethylation to the free sugar, and the last two derivatives were further characterised by the rotation of the derived lactone. 2 : 4-Di-*O*-methyl-D-galactose and free galactose were isolated as crystals. 2 : 4-Di-*O*-methyl-L-arabinose, 2-*O*-methyl-L-arabinose, and 3-*O*-methyl-L-arabinose were detected by chromatographic mobility, rotation, demethylation and rotation of the derived lactone. Crystalline L-arabinose was also isolated. 2 : 3 : 4-Tri-*O*-methyl-D-xylose and 2 : 3-di-*O*-methyl-D-xylose were shown to be present by chromatography and rotation and the latter

[11] Connel, Hirst, and Percival, *J.*, 1950, 3500.
[12] Chanda and Percival, *Nature*, 1950, **166**, 787.
[13] Buchanan, Percival, and Percival, *J.*, 1943, 51.
[14] Adams, Bishop, and Hughes, *Canad. J. Chem.*, 1954, **32**, 999.
[15] Cook and Smith, *Arch. Biochim. Biophys.*, 1953, **45**, 232; Cook, Neal, and Smith, *ibid.*, 1954, **53**, 192.
[16] Bera, Foster, and Stacey, *J.*, 1955, 3788.
[17] Percival, *Quart. Rev.*, 1949, **3**, 369.
[18] Buchanan and Percival, *Nature*, 1940, **145**, 1020.

also by demethylation. 4-*O*-Methyl-L-rhamnose was isolated as crystals with the correct melting point and rotation, and a mixture of 2 : 4- and 3 : 4-di-*O*-methyl-L-rhamnoses was also obtained.

The isolation of tetra-*O*-methylgalactose shows that some of the galactose functions as end-units, while the 2 : 3 : 5-tri-*O*-methyl derivative reveals the presence of galactofuranose residues linked through positions 1 and 6 in the polysaccharide. The monomethyl derivative and the free galactose could arise from galactose residues situated in a main chain and at branch points, as such residues, if they carried sulphate groups, would have at the most one hydroxyl group free for methylation. The occurrence of 2 : 4-di-*O*-methyl-L-arabinose shows that some of the arabinose occurs in the pyranose form with 1 : 3-linkages. The relatively large amounts of monomethyl and free arabinose isolated suggests that this sugar originates mainly from inner chains or at branch points. Trimethylxylose must arise from xylose that functions as end units, and the 2 : 3-di-*O*-methyl derivative may arise from 1 : 4-linked units of the branch chains or from end units which carry a sulphate residue on $C_{(4)}$. Apart from the presence of the relatively small quantity of the 3 : 4-di-*O*-methylrhamnose the other derivatives isolated indicate that this sugar is joined in the main by $C_{(1)}$ and $C_{(3)}$ linkages in the polysaccharide.

It may be that some of the hydroxyl groups of the monomethyl and free sugars isolated from the hydrolysate of the methylated polysaccharide escaped methylation because of the shielding effect of the sulphate groups. Furthermore the polysaccharide is bound up with protein or peptide material and this too may hinder complete methylation of the sugar residues. On the other hand the methylation results are supported by partial hydrolysis and periodate studies.

Proof that arabinose, xylose, and galactose occur as adjacent units in a single polysaccharide was obtained by the separation, after partial hydrolysis of material (A), of di- and tri-saccharides containing these three sugars. In addition the separation from this hydrolysate of oligosaccharides containing solely arabinose indicates the presence of several contiguous arabinose residues in the polysaccharide materials. Evidence that these oligosaccharides were not artefacts was obtained by the lack of formation of oligosaccharides when a synthetic mixture of the same sugars was subjected to identical hydrolysis (a small quantity of sulphuric acid being added comparable to that liberated from the ethereal sulphates) and separation procedures.

Oxidation of material (A) by sodium metaperiodate for 48 hr. gave an oxopolysaccharide in high yield. Quantitative analysis of the sugars in the hydrolysate from this material showed the almost entire elimination of xylose and the removal of about two-thirds of the galactose, indicating that these units contain two vicinal hydroxyl groups. That this is possible for 1 : 4-linked xylose and for galactose and xylose residues occurring as end units in the polysaccharide molecule is further support for the results of methylation. Arabinose, glucose, and rhamnose showed a relative increase in quantity in the oxopolysaccharide hydrolysate. This is in agreement with the methylation results; two contiguous methylated hydroxyls were not found in any of the methylated arabinoses and only a trace quantity of such a rhamnose derivative, namely, the 3 : 4-dimethyl compound, was isolated.

Subjection of the oxopolysaccharide from material (A) to mild acid hydrolysis followed by dialysis gave a residual polymer (X; SO_4, 19·95%) which revealed a single spot on an electrophoretogram when sprayed with toluidine-blue. Chromatographic analysis of the hydrolysate of the polymer (X) revealed the presence of mainly arabinose together with some galactose. The high sulphate content makes it clear that at least some of the arabinose must be sulphated, while the presence of arabinose and galactose is a further indication that they constitute the inner portion of the molecule. The hydrolysate from material (X) was also contaminated with glucose from the unremoved glucose-rich fraction.

All the results indicate that the glucose-free material has a highly branched structure consisting mainly of arabinose and galactose residues, the ends of the branches being

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terminated by galactose and xylose units. However the failure to separate this material into more than a single polysaccharide does not, in the authors' opinion, constitute definite proof of its homogeneity. It is probable that differentiation of a mixture of sulphated polysaccharides into single entities is impossible with the techniques that are available at present. For this reason no attempt has been made to advance a unique structure for this material.

The small glucose-rich fraction which was separated was devoid of nitrogen, contained less than 3% of sulphate, and gave no colour with iodine. It was essentially resistant to periodate attack since glucose was found in the oxopolysaccharide hydrolysate in relatively increased amount (6·6 compared with 3%). Partial hydrolysis of material (A) gave two glucose-containing oligosaccharides: one (R_{gal} 0·81) was chromatographically and electrophoretically identical with laminaribiose, while the other moved at a rate (R_{gal} 0·69) suggestive of a trisaccharide. No oligosaccharide containing glucose joined to any other sugar was isolated. On treatment of the extract (A) with β-glucosidase, an enzyme specific for β-glucosidic linkages, glucose was the only sugar liberated. Taken as a whole the evidence strongly suggests that the glucose-containing fraction is the β-1 : 3-linked glucan, laminarin. That this polysaccharide might be present in green seaweeds is not unlikely in view of its wide occurrence in the brown weeds.[19]

Experimental

Evaporations were carried out at 40° under reduced pressure. Paper-partition chromatography was done on Whatman No. 1 filter paper with the upper layers of the following solvent systems (v/v): (1) butan-1-ol–ethanol–water (5 : 4 : 1), (2) butan-1-ol–acetic acid–water (4 : 1 : 5), (3) ethyl acetate–pyridine–water (10 : 4 : 3), (4) benzene–butan-1-ol–pyridine–water (1 : 5 : 3 : 3). Electroionophoresis was carried out on a water-cooled apparatus [20] with Whatman No. 1 paper in an 0·1N-borate buffer at pH 10, 1 hr. being allowed for equilibration. After 4 hours' running (500 V; 12·5 mA) the paper was air-dried and the sugars were located by aniline oxalate–5% acetic acid spray. Demethylations were carried out by hydrobromic acid (*d* 1·46—1·49) in a sealed tube at 100° for 5—10 min., followed by addition of ethanol, neutralisation (silver carbonate), concentration to dryness, and extraction with ethanol; the demethylated sugars were identified by paper chromatograms.

Preparation of the Polysaccharide.—The seaweed was kindly collected, during July and November 1953, by the Institute of Seaweed Research, Inveresk, from rock pools midway between high and low tide near Dunbar. The whole weed (500 g.) was freed from extraneous matter by washing with cold running water for 12 hr., and, after removal of some of the colouring matter by treatment with cold alcohol (2·5 l.), was dried in a vacuum-desiccator for 3 days. Two extractions of a sample of this dried material (43 g.) with boiling water (6·5 l.) or with dilute hydrochloric acid (pH 3—4; 6 l.) for 4 hr. at 70° and concentration of the filtered extract to small volume gave a light green viscous solution. Adding this slowly, with stirring, to excess of ethanol precipitated a cream-coloured powder. This material, dried over phosphoric oxide at 50°/15 mm. to constant weight (4·9 g., *i.e.*, 11·4% of the cleaned dry weed), contained 3·4% of nitrogen. Direct Kjeldahl distillation, without prior digestion, showed the absence of salts of volatile bases. Acid hydrolysis followed by paper chromatography showed the absence of amino-sugars, but the presence of a number of amino-acids was detected (ninhydrin spray). Preferential removal of either protein or polysaccharide from the mixture with cadmium hydroxide,[1] with basic lead acetate,[2] with picric, phosphotungstic,[3] or phosphomolybdic acids, with debasing resin (Zeo-Karb 215), with copper chloride,[4] with Fehling's solution,[5] with zinc sulphate–sodium hydroxide,[6] and with ammonium sulphate [7] were investigated. All these attempts gave low recovery of polysaccharide with a nitrogen content of at least 2%. An attempt to reduce the nitrogen content by the action of the proteolytic enzymes papain and pepsin was unsuccessful. It was found that a 4% solution of trichloroacetic acid [8] constituted the most economical and efficient protein precipitant. Various scales of working were examined,

[19] Kylin, *Kgl. Fysiograf. Sällskap, Lund, Forh.*, 1944, **14**, No. 18.

and the following procedure was finally adopted. To an aqueous solution of the crude extract (1—1·5% w/v) was added a concentrated solution of trichloroacetic acid sufficient to give a final concentration of 4% (w/v). After several days at room temperature the fine precipitate was removed by centrifugation and the clear solution dialysed to neutrality (3 weeks). The polysaccharide was isolated (60—65% yield from the crude extract) by freeze-drying or by alcohol precipitation. The nitrogen content varied between 1·4 and 1·6%, and was not further reduced either by a second treatment with acid at 4% concentration or at various other concentrations (4—10%). Subsequent treatment with basic lead acetate or with chloroform and butan-1-ol [9] gave a very poor recovery of polysaccharide and failed to reduce the nitrogen content below 1%. This was, however, lowered with reasonable yield of material by fractional ethanolic precipitation of the polysaccharide from aqueous solution. After removal of the first fractions (50%, 70% alcohol; N, 2·0, 1·8% respectively) the supernatant liquor was evaporated to small volume and the polysaccharide (A) (2·8 g. from 43 g. of cleaned dried weed) precipitated as an off-white powder by pouring into excess of alcohol. It had $[\alpha]_D^{20}$ +69° (*c*, 1·0 in H_2O) [Found: N, 1·26; Ac, 0; OMe, 0; ash (direct), 13·7; (as sulphate) 16·1; Ca, 3·5; Fe, 0·7; Na, 0·6; K, trace; insoluble residue (Al_2O_3 + SiO_2), 0·9; SO_4 in ash, 10·0; total SO_4, 19·6%]. The sulphate content was not reduced by prolonged dialysis of an aqueous solution of material (A) against running water. While cations such as Ca^{2+} could be precipitated, no SO_4^{2-} could be detected in solutions of the polysaccharide until after hydrolysis. An aqueous solution of material (A) was non-reducing to Fehling's solution, gave a faintly reddish colour on treatment with iodine solution and a red colour only after treatment overnight with Selivanoff reagent. No evidence for the presence of ketose or anhydro-sugar residues was given with anthrone reagent.[21]

Hydrolysis of the polysaccharide at 100° with (*a*) N-sulphuric acid for 4 hr. or (*b*) 4N-sulphuric acid for 5 hr. followed by neutralisation with barium carbonate and paper chromatography (solvents 1 and 4) gave spots corresponding to galactose, glucose, arabinose, xylose, and rhamnose (aniline oxalate spray). Spraying with urea oxalate and with anthrone reagent [21] gave no indication of ketose or anhydro-sugars. Examination of the acid hydrolysate with solvent 2 indicated absence of uronic acids * (naphtharesorcinol spray). Each of the extracts (including a cold-water extract) and fractions of the extracts and each of the products from the various purification procedures gave identical chromatograms. Spots corresponding to arabinose, galactose, xylose, rhamnose, and glucose were obtained in every sample examined in, as far as could be judged visually, the same relative proportions. Quantitative analysis of the hydrolysate with sodium metaperiodate [22] (solvent 4) gave arabinose 42, galactose 38, xylose 11·5, rhamnose 3·3—7·7, and glucose 3·0%. Concordant results were obtained in duplicate determinations, but rhamnose gave variable results within the range shown. Arabinose and galactose determined by the Nelson–Somogyi method [23] were 41 and 38% respectively. Material (A) (9 g.) was hydrolysed by 0·5N-oxalic acid (400 ml.) for 6 hr. at 100° in an atmosphere of carbon dioxide. The cooled, neutralised (calcium carbonate), filtered solution was evaporated to dryness in a current of carbon dioxide. The dried (P_2O_5) residue was extracted with ethanol, the extracts were evaporated to dryness, and the residue was re-extracted until the syrup (2·94 g.; $[\alpha]_D^{20}$ +59°, *c* 1·7 in H_2O; *N*, 0) was free from inorganic ions. A portion (2·01 g.) of this syrup was separated on a cellulose column [24] with butan-1-ol two thirds saturated with water as eluant. After 9·5 l. had been collected the eluant was changed to butanol saturated with water +5% of ethanol and after 13 l. had been collected the column was washed with water (6 l.). Each fraction was evaporated to dryness and the resulting syrup purified with charcoal–Celite. The following substances were separated: 1, The syrup (58·2 mg.), R_F 0·78 (pink spot), $[\alpha]_D^{20}$ +20·8° (*c* 0·9 in H_2O), n_D 1·4875, gave a positive Selivanoff test. 2, Crystallised (81·2 mg.), $[\alpha]_D^{19}$ +8·8° (*c* 1·2 in H_2O); the derived benzoylhydrazone, m. p. and mixed m. p. 179—181° (decomp.), characterised this fraction as L-rhamnose. 3, The syrup (40·7 mg.), R_F 0·39, gave a positive Selivanoff test. 4, The syrup (232 mg.) crystallised from methanol had m. p. and

* Since the completion of this work, decarboxylation of material A with 19% w/v hydrochloric acid by Dr. D. M. W. Anderson has indicated a uronic acid content of 4%.

[20] Foster, *Chem. and Ind.*, 1952, 1050.
[21] Johanson, *Nature*, 1953, **172**, 956.
[22] Hirst and Jones, *J.*, 1949, 1659.
[23] Somogyi, *J. Biol. Chem.*, 1952, **195**, 19.
[24] Hough, Jones, and Wadman, *J.*, 1949, 2511.

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mixed m. p. with α-D-xylose 144—144·5°, $[\alpha]_D^{19}$ +41° ⟶ +16° (*c* 0·9 in H_2O). The derived dibenzylidene dimethyl acetal,[25] after recrystallisation from methanol, had m. p. and mixed m. p. 210—211°. **5**, The crystals (585·5 mg.) had m. p. 154—154·5°, $[\alpha]_D^{20}$ +156° ⟶ +107° (*c* 1·3 in H_2O; 30 min.) (Found: C, 39·9; H, 6·5. Calc. for $C_5H_{10}O_5$: C, 40·0; H, 6·7%); this fraction was further characterised as essentially β-L-arabinose by conversion into the benzoylhydrazone,[26] m. p. and mixed m. p. 199—203° (decomp.). **6**, Crystallised from methanol (75·7 mg.), m. p. 148—150°, $[\alpha]_D^{18}$ +55·5° (*c*, 0·8 in H_2O); its identity as D-glucose was established by aerobic oxidation to gluconic acid by the specific enzyme D-glucose oxidase (notatin),[27] the rate of oxygen uptake being measured in a Warburg apparatus. **7**, The syrup (513·6 mg.), crystallised from methanol, had m. p. 165—166°, $[\alpha]_D^{19}$ +138 ⟶ +83·5° (*c* 1·2 in H_2O); its identity as α-D-galactose was further established by the preparation of the diethyl mercaptal,[28] m. p. and mixed m. p. 140—141° (Found: C, 41·8; H, 7·6; S, 21·9. Calc. for $C_{10}H_{22}O_5S_2$: C, 41·8; H, 7·7; S, 22·4%). **8**, The syrup (143 mg.) consisted of a mixture of oligosaccharides (41·6 mg. were obtained as a syrup from overlap of fractions). Total recovery from the column was 93·5%.

Attempted Fractionation of the Extract (A).—Polysaccharide fractions precipitated from aqueous solution at different concentrations of alcohol (50, 70, 85, and 95%) gave identical chromatograms on hydrolysis and had sulphate contents of 19·1, 19·8, 19·2, and 19·9% respectively.

A 1% solution of material (A) in borate buffer (pH 10) gave a schlieren diagram with a symmetrical peak (Dr. C. T. Greenwood).

Electroionophoresis of material (A) on paper[20] followed by spraying with toluidine-blue,[29] a reagent specific for sulphate residues, gave a single discrete spot.

A portion of material (A), after conversion into the sodium salt,[15] was dissolved in water (200 ml.; 0·24% solution) and treated with stirring at room temperature with sufficient solid potassium chloride to give a 0·25M-solution.[15] No precipitation occurred immediately, after 4 days, or on repetition of the experiment at 0·15, 0·50, and 0·66M-concentrations of potassium chloride.

A dilute aqueous solution of material (A) in a sodium acetate–acetic acid buffer (pH 5·0) was incubated at 35° with a β-glucosidase preparation from *Cladophora rupestris*. Samples of the solution were spotted on a chromatogram initially and after 0·5 hr., 1 hr., 1·5 hr., and then at 2-hourly intervals, an enzyme control being run concurrently. The papers were irrigated with solvent (3) and sprayed with ammoniacal silver nitrate.[30] A single spot corresponding to glucose appeared after 2 hr. The enzyme control gave no spots on the chromatogram.

Treatment of an aqueous solution of material (A) with cetyltrimethylammonium bromide[16] gave an insoluble complex which on hydrolysis showed arabinose, galactose, xylose, and rhamnose (paper chromatography). Concentration and hydrolysis of the supernatant liquor gave a syrup which consisted mainly of glucose with minute quantities of the other four sugars (paper chromatography).

Periodate Oxidation and Investigation of the Oxopolysaccharide.—An aqueous solution of the sodium salt of material (A) was treated with 0·1M-sodium metaperiodate, and the periodate uptake was determined at intervals by the method of Fleury and Lange.[31] When this had virtually ceased (36 hr.) one mole of periodate had been consumed by 347 g. of polysaccharide. After 48 hours' treatment the oxopolysaccharide was isolated by (*a*) dialysis against running water (3—4 weeks) and freeze-drying, and (*b*) reduction of the periodate and iodate with gaseous sulphur dioxide followed by precipitation with ethanol. The precipitate was dissolved in water and reprecipitated in ethanol until free from inorganic contaminants. Recovery from both methods was 80—87% (Found: SO_4, 20·2; N, 1·3%). Hydrolysis and quantitative estimation of the relative proportions of sugars present gave arabinose 61·4, galactose 16·6, xylose trace, rhamnose 10·2—15·4, and glucose 6·6%.

Alkaline Degradation of the Polysaccharide and of the Oxopolysaccharide.—Material (A) (520 mg.) was heated at 100° with N-sodium hydroxide (100 ml.). Samples were withdrawn at

[25] Breddy and Jones, *J.*, 1945, 738.
[26] Hirst, Jones, and Woods, *J.*, 1947, 1048.
[27] Keilin and Hartree, *Biochem. J.*, 1948, **42**, 230.
[28] Wolfrom, *J. Amer. Chem. Soc.*, 1930, **52**, 2466.
[29] Rickets, Saddington, and Walton, *Biochem. J.*, 1954, **58**, 532.
[30] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[31] Fleury and Lange, *J. Pharm. Chim.*, 1933, **17**, 196.

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intervals and the liberated sulphate was estimated as the barium salt. The percentage hydrolysis was calculated on an initial sulphate content of 19·6% :

Time of hydrolysis (hr.)	0·5	4	6	8
Hydrolysis of sulphate (%)	12·0	58·5	65·0	68·0

Material (A) (1·123 g.) and its derived oxopolysaccharide (1·820 g.) were treated with N-potassium hydroxide solution (100 ml.) at 95° in an atmosphere of nitrogen. Samples were withdrawn at intervals, dialysed free from extraneous ions against running water, evaporated to small bulk, and freeze-dried :

	Time of hydrolysis (hr.)	Recovery (%)	SO_4 content (%)	N content (%)
Material (A)	4	54	15·1	0·69
	8	51	13·2	0·60
Oxopolysaccharide	1	43	17·6	0·90
	3	37	14·1	0·50

As far as could be judged visually from chromatograms of the hydrolysates alkali-degradation effected no change in the relative proportions of the sugars in material (A) or in the oxopolysaccharide.

Partial Hydrolysis of the Polysaccharide and Oxopolysaccharide with Acid.—Material (A) (400 mg.) was kept at room temperature with 0·1N-oxalic acid solution (100 ml.). After one month a small quantity of galactose (paper chromatography) had been liberated. The solution was then heated at 50° in an atmosphere of carbon dioxide and samples were removed at intervals, neutralised (calcium carbonate) and analysed chromatographically (Table 1).

TABLE 1.

Duration of hydrolysis (hr.)	1	2	3	5	9
Galactose	××	××	××	××	××
Arabinose	—	—	×	××	××
Xylose	—	×	××	××	××
Rhamnose and glucose	—	—	—	—	××
Oligosaccharides	—	—	×	×	××

× = trace.

Material (A) and oxopolysaccharide therefrom (each *ca.* 350 mg.) were hydrolysed with 0·04N-sulphuric acid for 3 hr. at 90°. The solutions were neutralised and dialysed. Chromatography of the dialysates showed galactose, xylose, and a trace of arabinose from material (A), but the oxopolysaccharide dialysate showed general streaking down the paper. After further hydrolysis with N-sulphuric acid (2 hr. at 100°) clean spots for arabinose, rhamnose, and galactose were obtained. Chromatograms sprayed with toluidine-blue showed no sign of sulphated sugars.

The residual polysaccharides in the dialysis bags were dialysed against running water and isolated by freeze-drying. The polysaccharide (59 mg., 24%) on hydrolysis gave the original five sugars (paper chromatography). The oxopolysaccharide (X, 43 mg.; SO_4, 19·95%) gave a single spot (toluidine-blue) on the electrophoretogram, and on hydrolysis was shown to contain principally arabinose with much smaller amounts of galactose and glucose.

The acidity of a solution of material (A) (200 mg.), when treated with 0·014N-sulphuric acid (20 ml.) at 100°, increased to 0·021N during 7 hr.

Isolation of Oligosaccharides.—Material (A) (12 g.) was hydrolysed with 0·5N-oxalic acid (400 ml.) at 95° for 3 hr. The dialysate, after neutralisation with calcium carbonate, de-ionisation with Amberlite resin IR-120H, 4-OHB, and evaporation, gave a syrup (B) (10 g.). A portion of this was separated into two fractions on a charcoal–Celite column (50 : 50).[32] Fraction I (4 g.), eluted with water, contained monosaccharides and two fast-moving oligosaccharides. Fraction II (521 mg.), eluted with 15% aqueous ethanol, consisted of a series of oligosaccharides. Fraction I was separated on a cellulose column. After elution of the monosaccharides (butan-1-ol-saturated with water) the two oligosaccharides were eluted with ethanol. They both gave pink spots with aniline oxalate, had R_{gal} values (rate of travel relative

[32] Bacon and Bell, *J.*, 1953, 2528.

to galactose) of 0·87 (main component) and 0·97 [cf. 3-*O*-β-L-arabopyranosyl-L-arabinose, R_{gal} 0·78 which was run on the same paper (solvent 3)]. Both oligosaccharides gave only arabinose on further hydrolysis.

Fraction II was separated on a second charcoal–Celite column (3 × 40 cm.) at a constant temperature of 20°. The initial eluant was water containing 1% of ethanol at 30 ml./hr. The ethanol concentration was increased by 1% at 24 hr. intervals. Considerable overlapping of the constituents occurred. The oligosaccharides were separated finally by paper chromatography (solvent 3), as shown in Table 2.

TABLE 2.

Fraction	Wt. (mg.)	Colour of spot, aniline oxalate spray	R_{gal} (solvent 3)	Sugars on hydrolysis *
1	4·0	Pink	0·58	Arabinose
2	4·7	,,	0·68	Arabinose, xylose (1 : 1)
3	8·9	Brown	0·38	Arabinose, galactose, xylose (2 : 1 : 1)
4	5·7	*a*, ,,	0·29	Galactose
		b, ,,	0·69	Glucose
5	6·5	,,	0·58	Galactose, arabinose, xylose (1 : 1 : 1)
6	6·0	Pink	0·28	Arabinose
7	3·4	Brown	0·81	Glucose

* The proportions of sugars were estimated visually. Fraction 7 was chromatographically and electroionophoretically [32] identical with laminaribiose (solvents 1 and 4), and moved at the same rate as an authentic specimen of this disaccharide in the form of their *N*-benzylglycosylamines.[33]

A synthetic mixture of sugars (galactose 3·8 g., arabinose 4·2 g., xylose 1·2 g., rhamnose 0·5 g.) was treated with 0·5N-oxalic acid (400 ml.) and N-sulphuric acid (2·5 ml.) as in the preparation of syrup B (yield 8·7 g.). An aqueous solution of this syrup was allowed to percolate down the charcoal column used in the oligosaccharide separation. After the column had been left overnight at 20° graded elution, as before, gave monosaccharides (8·3 g.) from the aqueous eluant and (0·2 g.) from 10% and 50% aqueous-ethanolic eluants. No evidence of oligosaccharides was obtained.

Acetylation of the Polysaccharide.—The polysaccharide (19 g.), dispersed in formamide (150 ml.) in an " Ato-Mix " mixer at room temperature, was kept with pyridine (1 l.) and acetic anhydride (500 ml.) for 2 weeks at room temperature. The clear brown solution was diluted with ice-water and dialysed for 2—3 weeks. Concentration and freeze-drying gave a white powder (18·0 g.; Ac, 17·2%) which on dispersion in pyridine (70 ml.) at room temperature in the " Ato-Mix " mixer gave a clear brown jelly. This was kept with acetic anhydride (60 ml.) at room temperature for a week. Dialysis and freeze-drying gave the acetylated polysaccharide (17·8 g.; Ac, 19·4%). A third treatment with pyridine (50 ml.) and acetic anhydride (40 ml.) gave a recovery of 17·8 g. (Ac, 20·6; N, 1·4%). Repeated acetylation at room temperature and at higher temperatures failed to increase the acetyl content of the product. Precipitation by alcohol or acetone–ether (50 : 50) gave an acetylated polysaccharide difficult to purify. The acetylated material was extracted (Soxhlet) with chloroform, the extracts were evaporated to dryness, and the residue was washed with hot water and extracted with cold chloroform (3 × 10 ml.). The latter extracts, after evaporation to dryness, were saponified by warm dilute aqueous alkali. The solution was dialysed to neutrality, concentrated, and freeze-dried. The product (51·2 mg.), on acid hydrolysis, showed glucose with traces of galactose, arabinose, and xylose (paper chromatography). This glucan (SO_4 <3%; N, 0) gave no colour with iodine and had a periodate uptake [31] of 1 mole for 420 g. of glucan. The chloroform-insoluble acetate (16·5 g.) contained arabinose, galactose, xylose, and rhamnose in their usual proportions (chromatography of the hydrolysate) but was devoid of glucose.

Methylation of the Acetylated Polysaccharide.—The glucose-free acetylated polysaccharide (16·5 g.; Ac, 20·6%) was dispersed in water (400 ml.). Dimethyl sulphate (110 ml.) and 40% aqueous sodium hydroxide (120 ml.) were then added simultaneously, with stirring, during 6 hr. at <10° in nitrogen. Further quantities of dimethyl sulphate (110 ml.) and 40% alkali (120 ml.) were added dropwise daily for 5 days, and the mixture, after dialysis for 10 days against running water, was evaporated to small bulk. The methylation was repeated twice at room temperature. After a final dialysis for 3 weeks the polysaccharide was isolated, by freeze-drying, as an

[33] Bayly and Bourne, *Nature*, 1953, **171**, 385.

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off-white powder (9·9 g.; OMe, 19·6%). Two further methylations during 6 hr. at 45° followed by 2 hr. at 70° gave, after neutralisation with acetic acid, dialysis for 10 days, and freeze-drying, a white hygroscopic solid (6·9 g.) (Found: OMe, 25·1; N, 0·6; SO_4^{2-}, 16·2; ash as sulphate, 8·3%), $[\alpha]_D^{21}$ +92° (*c* 4·0 in H_2O). This material was soluble in hot water and to a slight extent in chloroform. A hydrolysate of the chloroform extract (OMe, 26·1%) was chromatographically indistinguishable from that of the chloroform-insoluble residue (OMe, 24·8%).

Attempts to raise the methoxyl content by methylation with Purdie reagents, with thallous hydroxide and methyl iodide,[34] and by dispersion in dimethylformamide [35] were unsuccessful.

Hydrolysis of the Methylated Polysaccharide.—The methylated polysaccharide (6·0 g.) was heated with 5% methanolic hydrogen chloride (200 ml.) for 6 hr. The solution which was too dark for polarimetric readings was neutralised with silver carbonate and concentrated to a syrup. Hydrolysis with 0·5N-hydrochloric acid (200 ml.) for 3 hr. at 95°, neutralisation as before, and deionisation [hydrogen sulphide, then Amberlite resins IR-100(H) and IR-4B(OH)] gave a syrup which was thrice purified by dissolution in alcohol (40 ml.), filtration, and evaporation (yield 4·18 g.). This syrup was separated on a cellulose column (85 × 2·7 cm.) with light petroleum (b. p. 100—120°)–butan-1-ol (7 : 3 v/v) saturated with water. After 10 l. had been collected the ratio of the solvents was gradually changed first to 1 : 1 (v/v) and then, after another 6 l. had passed, to butan-1-ol saturated with water. Twenty-three fractions were separated, nine of which were mixtures due to overlap. The remaining fractions required purification and many of them were re-separated on paper. The overall recovery from the column was 85% but the weights recorded for the individual fractions are those obtained after repeated purification by treatment with activated charcoal in boiling alcohol or hot water, followed by alternate extraction of the resulting syrup with alcohol and water and concentration after each extraction.

Fraction 1. The syrup (75 mg.), R_G 0·94 [Solvent (1) for all methylated sugars], was a mixture of 2 : 3 : 5-tri-*O*-methylarabinose (trace) and 2 : 3 : 4-tri-*O*-methylxylose. Separation on paper [benzene–ethanol–water (169 : 47 : 15)] and purification gave a syrup (14 mg.), $[\alpha]_D^{18}$ +13° (*c* 0·8 in H_2O) (cf. 2 : 3 : 4-tri-*O*-methylxylose, $[\alpha]_D$ +18°).[36]

Fraction 2. The syrup (30·9 mg.) had $[\alpha]_D^{19}$ +106° (*c* 0·3 in H_2O), R_G 0·88 (Found: OMe, 50·8. Calc. for a tetramethylhexose: OMe, 52·5%), and was chromatographically identical with 2 : 3 : 4 : 6-tetra-*O*-methylgalactose. Demethylation gave galactose.

Fraction 3. The syrup (24 mg.) had $[\alpha]_D^{18}$ +8° (*c* 0·6 in H_2O), R_G 0·88, and corresponded to a dimethylrhamnose (chromatography). Electroionophoresis showed two components one moving at the same rate as 3 : 4-di-*O*-methylrhamnose, and the other stationary. Demethylation gave rhamnose. (Cf. 2 : 4-di-*O*-methyl-L-rhamnose, $[\alpha]_D$ −19°;[37] 3 : 4-di-*O*-methyl-L-rhamnose, $[\alpha]_D$ +18·6°;[30] 2 : 3-di-*O*-methyl-L-rhamnose, $[\alpha]_D$ +42·5°.[39])

Fraction 4. The syrup (60·2 mg.) had $[\alpha]_D^{18}$ −3·8° (*c* 0·9 in H_2O), R_G 0·86 (Found: OMe, 40·9. Calc. for $C_9H_{16}O_6$: OMe, 41·9%), and gave galactose on demethylation. Conversion into the lactone gave a syrup (13 mg.), $[\alpha]_D^{18}$ −29° (*c* 0·6 in H_2O) (cf. 2 : 3 : 5-tri-*O*-methyl-D-galactose, $[\alpha]_D$ −5°;[40] 3 : 4 : 6-tri-*O*-methyl-D-galactose, $[\alpha]_D$ −4·3°;[41] 2 : 3 : 5-tri-*O*-methyl-D-galactonolactone, $[\alpha]_D$ −32°;[40] 3 : 4 : 6-tri-*O*-methylgalactonolactone, $[\alpha]_D$ +46·8°[41]).

Fraction 5. The syrup (41 mg.) had $[\alpha]_D^{18}$ +20° (*c* 1·1 in H_2O), crystallising very slowly. It was chromatographically and ionophoretically identical with 2 : 3-di-*O*-methylxylose [42] ($[\alpha]_D$ +23°) and gave xylose on demethylation.

Fraction 6. The syrup (235 mg.) had $[\alpha]_D^{18}$ +100° (*c* 1·3 in H_2O), R_G, 0·63. Chromatography (solvents 1, 3, and 4) and electroionophoresis gave a single spot corresponding to 2 : 3 : 4-tri-*O*-methylgalactose, but demethylation gave galactose and arabinose (Found: OMe, 38·6. Calc. for $C_9H_{18}O_6$: OMe, 41·9. Calc. for $C_7H_{14}O_5$: OMe, 34·8%) (cf. 2 : 3 : 4-tri-*O*-methylgalactose,[43] $[\alpha]_D$ +121°; 2 : 3-di-*O*-methyl-L-arabinose,[44] $[\alpha]_D$ +107°).

[34] Hirst and Jones, *J.*, 1938, 502.
[35] Kuhn, Löw, and Frischmann, *Angew. Chem.*, 1955, **67**, 32; *Chem. Ber.*, 1955, **88**, 1492.
[36] Hirst, Percival, and Wylam, *J.*, 1954, 195.
[37] E. E. Percival and Charalambous, *J.*, 1954, 2443.
[38] Laidlaw and Percival, *J.*, 1949, 1600.
[39] Brown, Hough, and Jones, *J.*, 1950, 1125.
[40] Luckett and Smith, *J.*, 1940, 1116.
[41] Levene and Meyer, *J. Biol. Chem.*, 1931, **92**, 257.
[42] Chanda, Percival, and Percival, *J.*, 1952, 260.
[43] Levene and Kreider, *J. Biol. Chem.*, 1937, **121**, 155.
[44] Hirst and Jones, *J.*, 1948, 2311.

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Fraction 7. The syrup (27 mg.) crystallised and had $[\alpha]_D^{18}$ +15° (*c* 1·4 in H_2O),[45] R_G 0·57, m. p. and mixed m. p. with 4-*O*-methylrhamnose ($[\alpha]_D$ +13°) 122°.

Fraction 8. The syrup (33 mg.) had $[\alpha]_D^{18}$ +101° (*c* 1·6 in H_2O), R_G 0·54, and gave arabinose on demethylation. The derived lactone had $[\alpha]_D$ +88° ⟶ +40° (*c* 0·4 in H_2O) (cf. 2 : 4-di-*O*-methyl-L-arabinose,[46] $[\alpha]_D$ +118°; 2 : 4-di-*O*-methyl-L-arabonolactone,[47] $[\alpha]_D$ +99° ⟶ +39°).

Fraction 9. The syrup (539 mg.) had $[\alpha]_D^{18}$ +101° (*c* 2·0 in H_2O), R_G 0·38, and was chromatographically and electroionophoretically identical with 2-*O*-methylarabinose (Found : OMe, 18·0. Calc. for $C_6H_{12}O_5$: OMe, 18·9%). Demethylation gave arabinose. The derived lactone had $[\alpha]_D$ −38° (*c* 1·1 in H_2O) (cf. 2-*O*-methyl-L-arabinose,[48] $[\alpha]_D$ +100°; 2-*O*-methyl-L-arabonolactone,[44] $[\alpha]_D$ −44° ⟶ −40°).

Fraction 10. The syrup (32 mg.), R_G 0·38, was chromatographically and ionophoretically identical with 2 : 4-di-*O*-methylgalactose, and crystallised. After recrystallisation from ethyl acetate it had m. p. and mixed m. p. 80° (the recorded m. p. for this derivative [49] is 98—99° but authentic specimens in our possession all melted at 78—80°).

Fraction 11. The syrup (51·5 mg.) had $[\alpha]_D^{18}$ +112° (*c* 1·5 in H_2O), R_G 0·28, and was chromatographically and electroionophoretically identical with 3-*O*-methyl-L-arabinose. Demethylation gave arabinose. The derived lactone had $[\alpha]_D^{18}$ −65° (*c* 0·6 in H_2O) (cf. 3-*O*-methyl-L-arabinose, $[\alpha]_D$ +110°; derived lactone [50] −74°).

Fraction 12. The syrup (113 mg.) had $[\alpha]_D^{17}$ +78° (*c* 1·5 in H_2O), R_G 0·21, was chromatographically and electroionophoretically identical with 2-*O*-methylgalactose and gave galactose on demethylation. The derived lactone had $[\alpha]_D^{18}$ −18° (*c* 0·5 in H_2O) (cf. 2-*O*-methylgalactose, $[\alpha]_D$ +80°; derived lactone [51] $[\alpha]_D$ −27 ⟶ −24°).

Fraction 13. The syrup (303 mg.), R_G 0·14, chromatographically identical with arabinose, crystallised from methanol, then having m. p. and mixed m. p. with β-L-arabinose 154°, $[\alpha]_D^{18}$ +195° ⟶ +106° (*c* 1·2 in H_2O).

Fraction 14. The syrup (498 mg.), R_G 0·08, chromatographically identical with galactose, crystallised from methanol, then having m. p. and mixed m. p. with α-D-galactose 164—166°, $[\alpha]_D^{19}$ +130 ⟶ +81° (*c* 1·4 in H_2O).

The authors thank Miss B. Guarco for the fractionation with cetyltrimethylammonium bromide, Dr. C. T. Greenwood for the electrophoresis, and Dr. D. Manners for the determination of glucose with notatin and for the gift of β-glucosidase. They are grateful to Professor E. L. Hirst for his interest and advice, the Institute of Seaweed Research for the collection of the weed, and the Distillers Company Limited and Imperial Chemical Industries Limited for grants.

Department of Chemistry, University of Edinburgh. [*Received, February 8th*, 1957.]

[45] Levene and Compton, *J. Biol. Chem.*, 1936, **114**, 9.
[46] Andrews, Ball, and Jones, *J.*, 1953, 4090.
[47] Jones, *J.*, 1953, 1672.
[48] Jones, Kent, and Stacey, *J.*, 1947, 1341.
[49] Andrews, Hough, and Jones, *J.*, 1954, 806.
[50] Hirst, Jones, and Williams, *J.*, 1947, 1062.
[51] Hirst and Jones, *J.*, 1946, 506.

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518. *The Orton Rearrangement. Part III.* Evidence for the Mechanism Derived from Kinetic Studies of o-Substituted N-Bromoacetanilides.*

By M. J. S. Dewar and J. M. W. Scott.

The rearrangements of *N*-bromo-2-fluoro-, -2-chloro-, -2-nitro-, -2-phenyl-, -2-methyl-, and -2 : 6-dimethyl-acetanilide in chlorobenzene containing trichloroacetic acid have been studied kinetically, and also the analogous debromination of *N*-bromo-2 : 4 : 6-trichloroacetanilide. In several cases chemical and kinetic evidence was found for the intervention of an intermediate containing active bromine. This supports the mechanism suggested by Israel, Soper, and Tuck,[1] and this mechanism is theoretically preferable to that involving π-complex intermediates.[2]

The Orton rearrangement is a rearrangement of *N*-halogenoacylanilides in which the halogen migrates to a *para*- or occasionally an *ortho*-position in the ring. Such reactions have been effected under conditions of three types: (1) Photochemically or by the action of heat; these reactions probably involve free-radical intermediates. (2) With halogen acids as catalysts, the evidence[3] indicating that these reactions are intermolecular, involving as Orton suggested, free halogens as intermediates. (3) With carboxylic acids or phenols as catalysts in aprotic solvents. The present paper is concerned with reactions of the last type.

Bell and his collaborators[4–6] studied in detail the rearrangement of *N*-bromoacetanilide, *N*-bromobenzanilide, and *N*-iodoformanilide in aprotic solvents, using a variety of carboxylic acid and phenols as catalysts. They found that the rearrangements were of first order with respect to the *N*-halogenoacylanilide and obeyed the Brönsted relation. They also established that the reactions did not take place by the Orton mechanism (involving free halogen as intermediate), and Bell[6] concluded that they were probably intramolecular.

On the other hand Israel, Soper, and Tuck[1] considered the reactions to be intermolecular, proceeding by a variation of the Orton mechanism in which an acyl hypohalite is the intermediate; *i.e.*:

$$\mathrm{Ph{\cdot}NXAc + HOY \longrightarrow Ph{\cdot}NHAc + XOY}$$
$$\mathrm{Ph{\cdot}NHAc + XOY \longrightarrow X{\cdot}C_6H_4{\cdot}NHAc + HOY}$$

where X is the halogen and HOY the acid catalyst. They observed that when *N*-bromoacetanilide was allowed to react with acetic acid in presence of anisole or phenetole, most of the bromine migrated to the ether. This they considered to be evidence for an intermolecular mechanism. It is, however, inconclusive, for two reasons. First, the migration of bromine to the added ether might have involved a direct bromination of the ether by the *N*-bromoamide, and it would then throw no light on the rearrangement since the mechanisms of the two processes would be dissimilar.† Secondly, if the rearrangements are intermolecular, it seems very likely that they take place through a π-complex which

* Part II, *J.*, 1957, 1445.

† Mr. P. Couzens, in these laboratories, has recently shown that the bromine transfer does take place mainly in this way.

[1] Israel, Soper, and Tuck, *J.*, 1945, 547.

[2] Dewar, "Electronic Theory of Organic Chemistry," Oxford, 1949, p. 168.

[3] For reviews and references see Hughes and Ingold, *Quart. Rev.*, 1952, **6**, 34; Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 604.

[4] Bell, *Proc. Roy. Soc.*, 1934, *A*, **143**, 377; Bell and Levinge, *ibid.*, 1935, *A*, **151**, 211; Bell and Dankwerts, *J.*, 1939, 1774; Bell and Lidwell, *J.*, 1939, 1096.

[5] Bell and Brown, *J.*, 1936, 1520.

[6] Bell, *J.*, 1936, 1154.

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would be expected to act as a brominating agent and might well brominate any reactive compound such as anisole that might be present.

The available evidence concerning the mechanism of the Orton rearrangement in aprotic solvents is therefore still inconclusive, and there is not even a general consensus of opinion whether it is intramolecular or intermolecular. We have now obtained definite evidence that the reaction takes place in stages, through the formation of an intermediate brominating agent; this strongly supports the Soper mechanism.

Our evidence comes from a kinetic study of the rearrangements and related reactions of a number of *ortho*-substituted *N*-bromoacetanilides. It could be predicted that the steric effects of *ortho*-substituents would increase the life of the intermediate if the Soper mechanism operated, and we have detected formation of an intermediate in such cases.

Experimental

Materials.—" AnalaR " trichloroacetic acid solutions were prepared as previously described [7] and were standardised by addition of water and titration with sodium hydroxide to phenolphthalein. The 2- and poly-substituted *N*-bromoacylanilides were prepared as before; [7,8] their purity, determined by estimation of active bromine, ranged from 97 to 100%. The solutions of the *N*-bromoacylanilides were made up by volume, and concentrations checked by estimation of active bromine. The acid solutions were stored in a desiccator over anhydrous calcium chloride or silica gel. The *N*-bromoacylanilide solutions were stored in brown bottles over anhydrous calcium chloride or silica gel in a desiccator in the dark, and were stable for at least a year.

Table 1. *Reaction of* N-*bromo-2-nitroacetanilide* (I).

Temp. 25·1°							
Concn. of (I) (N) ...	0·0643	0·0648	0·0455	0·0385	0·0338	0·0134	0·0088
10^5k (sec.$^{-1}$)	2·49	2·49	2·51	2·65	2·70	3·44	3·53
	$10^5k_0 = 14·1$ sec.$^{-1}$.						
Temp. 35·7°							
Concn. of (I) (N) ...	0·0640	0·0471	0·0415	0·0358	0·0299	0·0245	0·0131
10^5k (sec.$^{-1}$)	6·12	6·34	6·50	6·50	6·78	7·15	7·70
	$10^5k_0 = 31·2$ sec.$^{-1}$.						
Temp. 44·5°							
Concn. of (I) (N)	0·0640	0·0471	0·0415	0·0358	0·0229	0·0245	0·0191
10^5k (sec.$^{-1}$)	13·3	13·3	13·1	14·5	14·9	15·3	15·9
	$10^5k_0 = 66·5$ sec.$^{-1}$.						
	$E = 15·5$ kcal. mole^{-1}. log $PZ = 6·4$.						

Rate Measurements.—The conventional thermostat was kept constant within ±0·02°. The reaction vessels were essentially the same as those used by Bell and Levinge.[4] The mercury seal was rarely used. The reaction vessels were covered with tin-foil during the runs. The runs were initiated by mixing equal volumes (25 ml.) of acid and *N*-bromoacylanilide solutions after both had come to equilibrium in a thermostat. The rearrangement was followed by estimation of active bromine. The first-order constants were obtained graphically or by the method of least squares.

N-*Bromo-2-nitroacetanilide.*—Under the conditions used this anilide does not rearrange but brominates the solvent.[8] The reactions were carried out in 0·279N-acid, and followed first-order kinetics with respect to anilide. The first-order constants (k) varied, however, with the initial concentration of anilide, in a manner analogous to that found by Bell and Levinge [4] for *N*-bromoacetanilide. The empirical relation suggested by those authors was used to give a limiting first-order constant, and from this the limiting constant k_0, corresponding to unit acid concentration, was calculated. The values of k and k_0 at three temperatures are given in Table 1, together with the Arrhenius parameters calculated from the values of k_0.

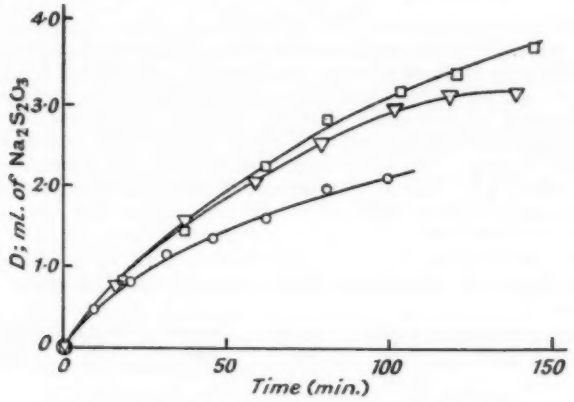
[7] Dewar and Scott, *J.*, 1957, 1445.
[8] *Idem*, *J.*, 1955, 1845.

N-*Bromo-2-methylacetanilide.*—Rearrangement was carried out in 0·358N-acid. The first-order constants determined graphically did not demonstrate any systematic variation with the initial concentration of the *N*-bromoacylanilide. The variation was shown to be random by recalculating the first-order constants by the method of least squares. These constants are given in Table 2, together with values for k_0 and the Arrhenius parameters.

After the above investigations it was decided to investigate the rates at fewer initial concentrations.

N-*Bromo-2-chloro-* and *-2-phenyl-acetanilide.*—With these compounds the titrations became erratic. Investigation showed that if aliquot parts of reactant were titrated rapidly after addition of iodide solution, reproducible end-points could be obtained; but soon iodine was slowly liberated. After 2—4 hr. a second stable end-point was reached. Clearly the *N*-bromo-

FIG. 1. *Concentration of intermediate plotted against time, for* N-*bromo-2-phenylacetanilide.*



Anilide concn. : □ 0·0595N, ▽ 0·0279N, ○ 0·0205N.

amides, which react rapidly with iodide, are converted into other oxidising agents which react slowly. That this oxidation was due to some substance in the chlorobenzene layer was shown by titration without agitation; the formation of free iodine took place at the interfaces between the chlorobenzene and the aqueous phase.

These agents accumulated during the reaction as shown in Fig. 1; here *D* represents the

TABLE 2. *Rearrangement of* N-*bromo-2-methylacetanilide* (II).

Temp. :	20·1°	35·85°	45·25°	Temp. :	20·1°	35·85°	45·25°
(II) (N)	10^5k (sec.$^{-1}$)	10^5k (sec.$^{-1}$)	10^5k (sec.$^{-1}$)	(II) (N)	10^5k (sec.$^{-1}$)	10^5k (sec.$^{-1}$)	10^5k (sec.$^{-1}$)
0·0655	0·247	1·10	2·35	0·0241	—	1·02	2·29
0·0460	0·238	1·02	2·24	0·0180	—	0·998	2·30
0·0410	—	0·990	2·27	0·0131	—	1·05	2·36
0·0361	—	0·983	2·21	10^5k (mean)	0·243	1·02	2·30
0·0305	—	0·986	2·35	10^5k_0	0·679	2·85	6·43

E = 16·6 kcal. mole^{-1}. log PZ = 7·1.

TABLE 3.

N-*Bromo-2-phenylacetanilide. Acid,* 0·282N.

Anilide	26·00°	34·80°	45°
(N)	10^5k (sec.$^{-1}$)	10^5k (sec.$^{-1}$)	10^5k (sec.$^{-1}$)
0·0595	1·16	2·26	5·89
0·0279	1·83	4·09; 4·06	9·31
0·0205	2·36	5·22	11·8

E = 14·9 kcal. mole^{-1}. log PZ = 6·6.

N-*Bromo-2-chloroacetanilide. Acid,* 0·282N.

Anilide	26°	34·8°	45°
(N)	10^5k (sec.$^{-1}$)	10^5k (sec.$^{-1}$)	10^5k (sec.$^{-1}$)
0·0595	1·58	2·44	5·78
0·0448	1·81	2·63; 2·68	5·35
0·0180	3·28	5·35	13·3

E = 14·7 kcal. mole^{-1}. log PZ = 6·3.

difference between the two titres—presumably equal to the concentration of the new oxidising agent. Over a long period, D passed through a maximum, and eventually the solution lost all its oxidising power; the rearrangement product could then be isolated.

Thus the rearrangement occurs in at least two stages, the new oxidising agent being formed as an intermediate.

Logarithmic plots (Fig. 2) showed that the disappearance of N-bromo-amide, as measured by the first (rapid) titre, X_o, followed a reaction first order in amide; the kinetics appeared similar

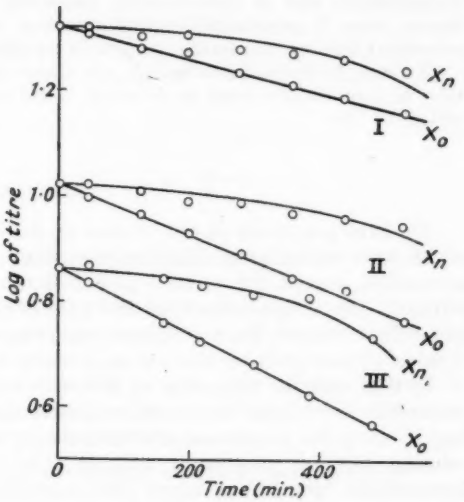


FIG. 2. *First-order plots for* N-*bromo-2-phenylacetanilide.*

Anilide concn.: I, 0·0595N, II, 0·0279N, IV, 0·0205N.

to those for the reactions of " normal " N-bromoacetanilide derivatives. The corresponding rate constants and Arrhenius parameters are in Table 3. The values for the second titre, X_n, are also indicated in Fig. 2.

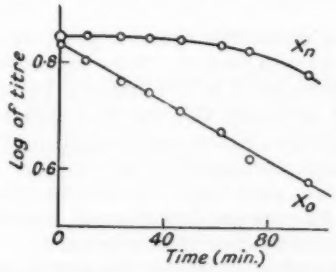


FIG. 3. *First-order plot for* N-*bromo-2 : 4 : 6-trichloroacetanilide.*

N-*Bromo-2-fluoro-* and N : 2-*Dibromo-acetanilide.*—Only the most concentrated solutions of N-bromo-2-fluoroacetanilide indicated production of the intermediate. No intermediate was found with N : 2-dibromobromoacetanilide. The kinetic results are in Table 4.

TABLE 4.

N-*Bromo-2-fluoroacetanilide. Acid*, 0·358N.				N : 2-*Dibromoacetanilide. Acid*, 0·358N.		
Anilide (N)	25° 10^5k (sec.$^{-1}$)	35·15° 10^5k (sec.$^{-1}$)	45° 10^5k (sec.$^{-1}$)	Anilide (N)	35·15° 10^5k (sec.$^{-1}$)	45° 10^5k (sec.$^{-1}$)
0·0569	1·69	3·94	9·09	0·0555	1·25	2·65
0·0336	1·66	4·08	9·20	0·0323	1·23	2·95
0·0083	—	4·80	9·59	0·0095	1·27	2·96
E = 13·9 kcal. mole^{-1}. log PZ = 5·7.				E = 17·8 kcal. mole^{-1}. log PZ = 7·2.		

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N-*Bromo*-2 : 4 : 6-*trichloroacetanilide*.—Since this bromo-amide cannot rearrange, it was thought that reaction with trichloroacetic acid in chlorobenzene might lead to a complete conversion into the intermediate, the second titre (X_n) remaining constant. This was approximately true for the first part of the reaction, as shown in Fig. 3; here again the disappearance of *N*-bromo-amide, measured by the first titre (X_o), follows first-order kinetics. Over a long period X_n decreased gradually to zero; *p*-bromochlorobenzene could then be isolated.[7] Then *N*-bromo-2 : 4 : 6-trichloroacetanilide (0·02M) was allowed to react with trichloroacetic acid in chlorobenzene containing acetanilide (0·05M). No intermediate was formed since it presumably rapidly attacked the acetanilide. No attempt was made to investigate this reaction further because of the difficulty of separating mixtures of anilides.

N-*Bromo*-2 : 6-*dimethylacetanilide*.—A single run was carried out with this compound at 45°; no intermediate could be detected. Acid concentration, 0·282N; anilide, 0·040N; $k = 4{\cdot}07 \times 10^{-7}$ (sec.$^{-1}$).

Discussion

We have previously shown [7, 8] that all the substituted *N*-bromoacylanilides discussed in this paper rearrange in chlorobenzene–trichloroacetic acid to the corresponding *p*-bromoacetanilide, except the *p*-nitro- and 2 : 4 : 6-trichloro-derivatives which brominate the solvent. The disappearance of the bromo-amide follows first-order kinetics, and the first-order constants show analogous variations with initial concentrations of the amides; it seems at least probable that all these reactions take place by a common mechanism.

In that case the behaviour of *N*-bromo-2-chloro-, -2-phenyl-, and -2 : 4 : 6-trichloroacetanilide shows that the overall reactions take place in at least two stages. The first step involves the production of a brominating agent which reacts only slowly with iodide solution, together presumably with an equivalent amount of the free acetanilide; the intermediate brominating agent then substitutes either the free acetanilide formed in the first step, or the solvent. Although we have not yet been able to isolate this intermediate, it seems entirely reasonable that it should be trichloroacetyl hypobromite, as required by the Soper mechanism.[1] Certain hypobromites have been reported [9] to react slowly with iodide in a two-phase system, presumably because they are almost insoluble in water.

The intermediate should only accumulate to an appreciable extent in cases where the second step in the Soper mechanism is slow compared with the first. Since the second step is an electrophilic substitution of an acetanilide derivative, it will be inhibited by positive substituents. Moreover *ortho*-substituents should accelerate the first step sterically, in which the bulky group NXAc is replaced by the less bulky NHAc, and sterically inhibit the second step by interfering with the coplanarity and conjugation of the ring and NHAc group. In fact we could detect the intermediate only when bulky *ortho*-substituents were present, and a methyl group ($-I$) was ineffective. Fluorine and bromine were less effective than chlorine; the former is smaller, and the latter less positive, than chlorine.

The behaviour of the 2-nitro-compound was surprising; it did not rearrange, it gave no intermediate, and the rate of acid attack was higher than for the other anilides investigated. It seems quite likely that the *o*-nitro-group increases the electrophilic nature of the bromine to such an extent that direct bromination of the solvent takes place. A similar reaction probably accounts for the bromine transfer observed by Israel *et al.*[1] when *N*-bromoacetanilide reacts in presence of anisole or phenetole.

Bell [6] observed that the rate of rearrangement of *N*-bromoacetanilide varied little with changes in the dielectric constant of the solvent. This suggests very strongly that no ions are formed as intermediates in the reaction. However the rate-determining step must be some reaction of the anilide with the acid catalyst, for otherwise the Brönsted relation would not be obeyed. These observations seem to indicate that the reaction must take

[9] Day and Taggart, *Ind. Eng. Chem.*, 1928, **20**, 545; Scott, *ibid.*, *Anal. Ed.*, 1931, **3**, 67.

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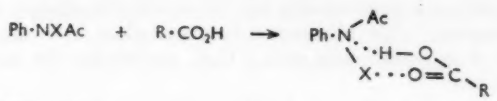
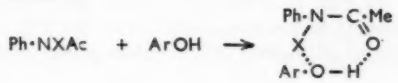
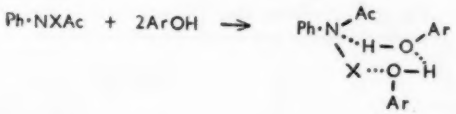
place through a cyclic transition state in which no integral charges need develop; *e.g.*, for a carboxylic acid,



and for a phenol, ArOH, either



or



A similar transition state can be written for hydrogen bromide; this would account for its extreme efficiency as a catalyst in aprotic solvents.[6]

It is not immediately apparent why a reaction of this type should obey the Brönsted relation; this aspect will be discussed in a later paper when it will be shown that the Brönsted relation should hold for such reactions.

It therefore seems highly probable that the rearrangements of all *N*-halogeno-compounds in aprotic solvents with carboxylic acids and phenols as catalysts take place by the Soper mechanism, but a further study of the reaction is in progress.

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519. *Four Higher Annellated Pyrenes with Acene Character.**

By B. BOGGIANO and E. CLAR.

The naphthopentacene (IV) has been synthesised from naphthalene-2 : 3-dicarboxylic anhydride and pyrene, the naphthohexacene (XIII) from anthraquinone-2 : 3-dicarboxylic anhydride and pyrene, and the dinaphthoheptacene (XVIII) from pyromellitic anhydride and pyrene. A benzonaphthotetracene was a by-product in another synthesis of the first product, (IV), from pyrene-3-carboxyl chloride and 6-methyltetralin and has been also prepared by a different route. These annellated pyrenes have been compared with the centrosymmetrically annellated pyrenes of the same number of rings and found to have acene character.

HIGHER, symmetrically annellated pyrenes retain their pyrene character, *i.e.*, they give pyrenequinones and their absorption spectra show the characteristic features of pyrene derivatives.[1] Strongly asymmetric linear annellated pyrenes have now been prepared in order to determine whether the pyrene character is still preserved or an acene character developed.

Naphthalene-2 : 3-dicarboxylic anhydride with pyrene in the presence of aluminium chloride gave the acid (I). Boiling benzoyl chloride and a trace of zinc chloride cyclised this to the quinone (II), which, like pentacenequinone and its angular benzologues, does

* The term "acene" denotes the series of linear annellated benzene derivatives beginning with anthracene, naphthacene (tetracene), pentacene (cf. Clar, *Ber.*, 1939, **72**, 2137).

[1] Clar, *J.*, 1949, 2013.

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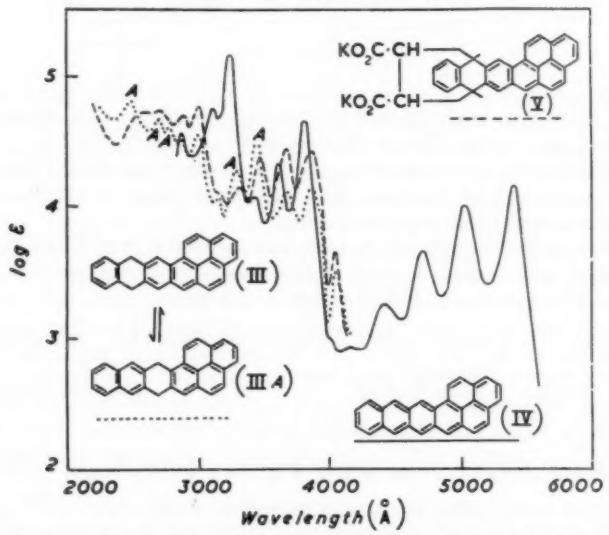
not give a vat. The quinone (II) was reduced to the dihydro-compound (III) with pyridine, zinc dust, and acetic acid. However, structure (III), consisting of a 3 : 4-benzopyrene complex linked to a benzene ring by two methylene groups, is not the only form of the dihydro-compound. The absorption bands marked "*A*" in Fig. 1 show clearly that the form (III) is in equilibrium with (III*A*), containing the aromatic complexes of pyrene and naphthalene.

Dehydrogenation of the compound (III) with palladium–charcoal yields the red naphthopentacene (IV; see Fig. 1), which is a rather reactive and photo-oxidisable. It adds maleic anhydride, leading to the formation of (V; see Fig. 1). When compared with that of the dihydro-compound (III⇌III*A*), the absorption spectrum of the adduct (Fig. 1)

FIG. 1. *Absorption max.* (Å) *and* log ε (*in parentheses*).



(——) *Naphthopentacene* (IV) *in* C_6H_6. 5410 (4·15), 5040 (4·00), 4720 (3·65), 4430 (3·25), 3820 (4·65), 3630 (4·33), 3440 (4·06), 3250 (5·15), 3110 (4·74), 2890 (4·56).
(– – – –) *Adduct* (V) *in* 50% EtOH, 4050 (3·64), 3870 (4·42), 3670 (4·42), 3470 (4·38), 3310 (4·16), 3010 (4·76), 2890 (4·70), 2720 (4·72), 2610 (4·71).
(. . . .) *Hydrocarbon* (III and III*A*) *in* EtOH, 4050 (3·50), 3880 (4·14), 3680 (4·12), 3440 (4·48), 3290 (4·27), 3150 (4·06), 3000 (4·54), 2870 (4·50), 2790 (4·60), 2680 (4·66), 2480 (2·80).

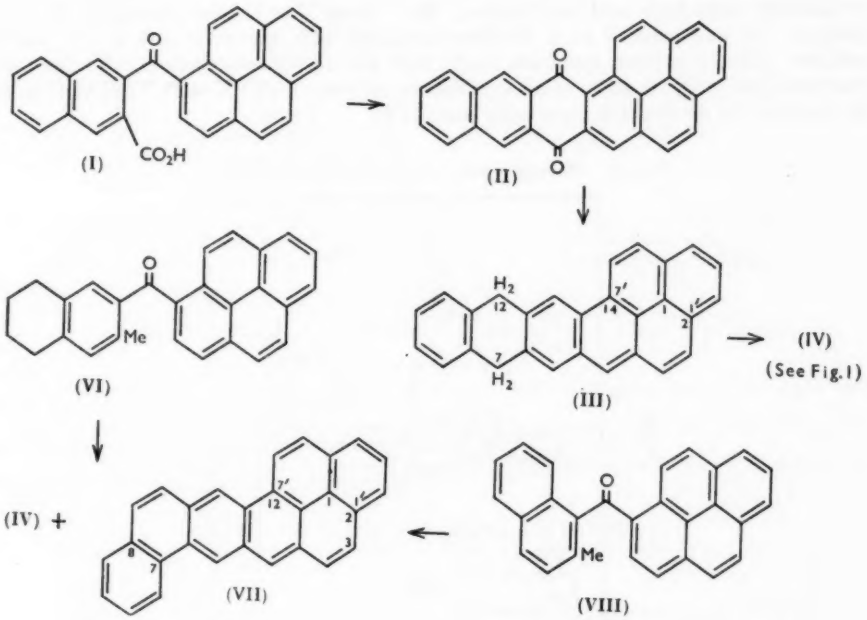
shows the correctness of the assumed structure (V). The first group of absorption bands of the red hydrocarbon (IV) (Fig. 1) is shifted considerably to the violet, relatively to the first bands of pentacene (5755 Å), as would be expected for an angular annellated benzologue of pentacene.

Pyrolysis of the ketone (VI), obtained from pyrenecarboxyl chloride and methyltetralin, also yields the red naphthopentacene (IV) together with a yellow hydrocarbon (VII), whose structure was established by synthesis from the ketone (VIII). Since "*cis*"-bis-angular dibenzanthracenes and tetracenes cannot be obtained from the corresponding *ortho*-methylated ketones by pyrolysis, owing to the preceding rearrangement of the ketone,[2] it must be assumed that the ketone (VIII) also rearranges and pyrolyses to the "*trans*"-bis-angular hydrocarbon (VII). The absorption spectrum of the compound (VII)

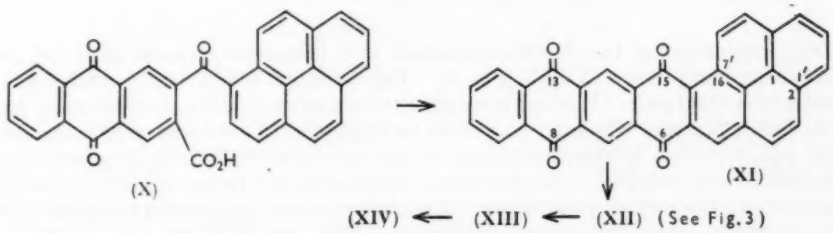
[2] Cook, *J.*, 1931, 499, 478; Clar, John, and Avenarius, *Ber.*, 1939, **72**, 2139; Clar, *Ber.*, 1943, **76**, 149; Nichol, Thorn, Jones, and Sandin, *J. Amer. Chem. Soc.*, 1947, **69**, 376.

is closely related to that of the naphthotetracene (IX; Fig. 2), the fusion of an angular ring to the latter causing a shift to the violet as usual.

The acid (X) was prepared from anthraquinone-2 : 3-dicarboxylic anhydride, pyrene, and aluminium chloride. It was cyclised with boiling benzoyl chloride to the diquinone (XI). Reduction in pyridine with zinc dust and acetic acid yielded a dihydro-compound



which, like (III ⇌ III*A*), consisted of an equilibrium mixture of isomers (XII) and (XII*A*) (Fig. 3). The absorption spectrum in Fig. 3 shows that the isomer (XII), containing the aromatic complexes of 3 : 4-benzopyrene and naphthalene, dominates the absorption spectrum, whilst the isomer (XII*A*), with the naphthopyrene (bands marked *A*) and benzene complexes, forms only about 10% of the mixture.



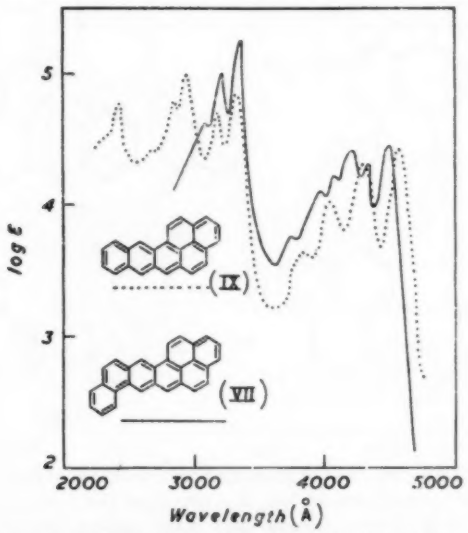
The naphthohexacene (XIII) (in Fig. 3) was obtained from its dihydro-compound by dehydrogenation with palladium–charcoal. Although highly reactive and photo-oxidisable, the green hydrocarbon is more stable than hexacene and a quantitative absorption spectrum can be obtained which shows the expected considerable violet shift compared with hexacene (Fig. 3). The compound adds maleic anhydride immediately,

XUM

leading to the adduct (XIV) (in Fig. 3), whose structure was established by comparison with the absorption spectrum of (XII ⇌ XII*A*) (Fig. 3).

Pyromellitic anhydride condensed twice with pyrene in the presence of aluminium chloride, to give the acid (XV) which might possibly contain the isomeric *iso*phthalic acid. Ring closure with benzoyl chloride gave an apparently uniform diquinone for which, in analogy with the formation of 1 : 2-8 : 9-dibenzopentacene-5 : 14-7 : 12-diquinone [3] from pyromellitic anhydride and naphthalene, the "*trans*"-bis-angular structure (XVI) is assumed. It was reduced to a dihydro-compound with zinc dust and acetic acid in pyridine. The absorption spectrum shows that the dihydro-compound, as in the cases described previously, consists of an equilibrium mixture of (XVII ⇌ XVII*A*) (Fig. 4), the bands of the asymmetric form being marked *A*.

FIG. 2. *Absorption max.* (Å) *and* log ε (*in parentheses*).



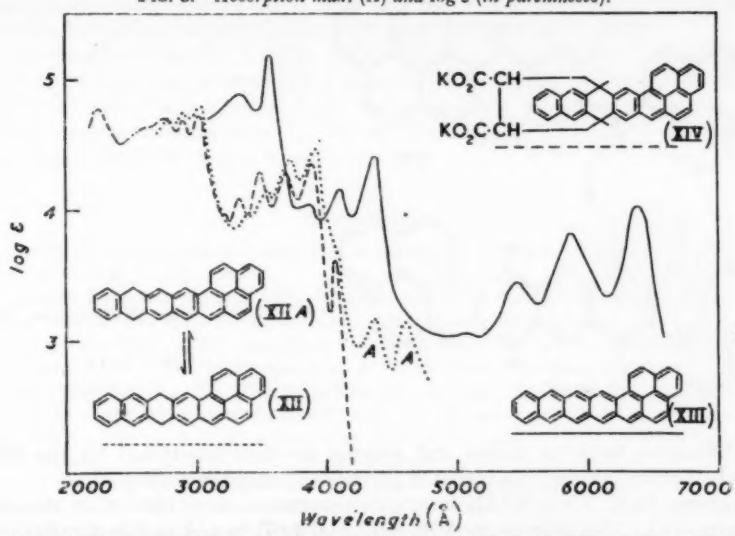
(——) *Hydrocarbon* (VII) *in* C_6H_6, 4500 (4·45), 4350 (4·31), 4230 (4·40), 4100 (4·20), 4000 (4·10), 3770 (3·75), 3370 (5·24), 3220 (4·98), 3100 (4·61).
(. . . .) *Hydrocarbon* (IX) *in* C_6H_6, 4580 (4·42), 4310 (4·31), 4060 (4·03), 3850 (3·63), 3350 (4·85), 3200 (4·70), 2970 (5·00), 2860 (4·78); *in* EtOH, 2460 (4·79).

Dehydrogenation of the dihydro-compound with palladium–charcoal gave the deep green dinaphthoheptacene (XVIII) (Fig. 4). This is the first fully aromatic benzologue of heptacene obtained pure. It is highly reactive and photo-oxidisable but considerably more stable than heptacene. Contrary to a claim by Baily and Liao [4] we have been unable to obtain pure heptacene by dehydrogenation of its hydro-compounds: the deep green crude heptacene always contained hydro-derivatives which could not be removed by sublimation or extraction; the very sensitive heptacene became even less pure during these operations until the green colour disappeared completely. Baily and Liao did not measure the purity of their heptacene by an absorption spectrum.

Dinaphthoheptacene adds maleic anhydride in solution, to form an endocyclic adduct. From the absorption spectrum the derived salt has the symmetrical structure (XIX) (Fig. 4).

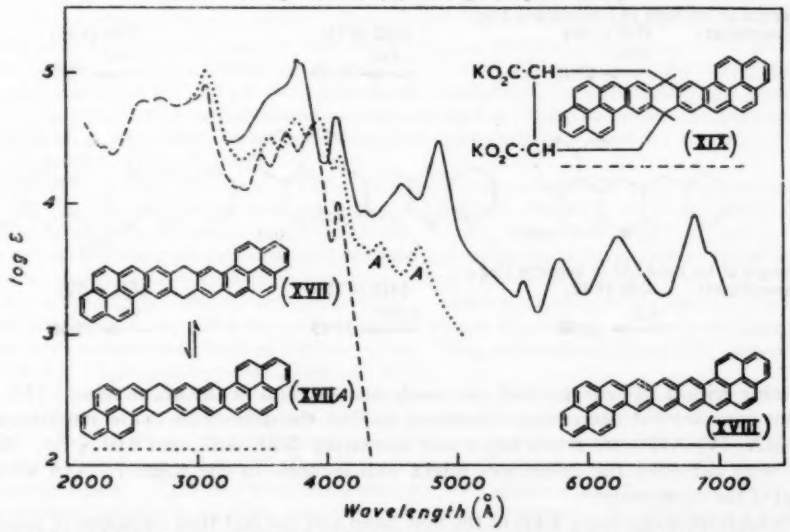
[3] Clar, *Ber.*, 1943, **76**, 257.
[4] Baily and Chien-Wei Liao, *J. Amer. Chem. Soc.*, 1955, **77**, 992.

FIG. 3. *Absorption max.* (Å) *and* log ε (*in parentheses*).



(——) *Naphthohexacene* (XIII) *in* $C_6H_3Cl_3$, 6390 (4·02), 5860 (3·82), 5460 (3·44), 4360 (4·40), 4100 (4·14), 3870 (4·04), 3580 (5·16), 3360 (4·87).
(– – – –) *Adduct* (XIV) *in* 50% EtOH, 4050 (3·59), 3880 (4·34), 3675 (4·28), 3490 (4·27), 3300 (4·06), 3020 (4·70), 2900 (4·68), 2740 (4·70), 2590 (4·62), 2230 (4·76).
(. . . .) *Hydrocarbon* (XII *and* XII*A*) *in* C_6H_6, 4600 (3·15), 4260 (3·18), 3920 (4·47), 3720 (4·40), 3530 (4·14), 3020 (4·80), 2900 (4·74), 2770 (3·68).

FIG. 4. *Absorption max.* (Å) *and* log ε (*in parentheses*).



(——) *Dinaphthoheptacene* (XVIII) *in* $C_6H_3Cl_3$, 6830 (3·90), 6240 (3·72), 5770 (3·56), 5500 (3·40), 4860 (4·48), 4570 (4·14), 4070 (4·66), 3780 (5·10).
(– – – –) *Adduct* (XIX) *in* 50% EtOH, 4070 (4·00), 3900 (4·60), 3690 (4·54), 3480 (4·34), 3320 (4·12), 3060 (4·90), 2940 (4·78), 2700 (4·81), 2590 (4·78), 2240 (4·42).
(. . . .) *Hydrocarbon* (XVII *and* XVII*A*) *in* $C_6H_3Cl_3$, 4675 (3·70), 4390 (3·70), 4090 (4·36), 3950 (3·70), 3750 (4·64), 3550 (4·52), 3080 (5·04).

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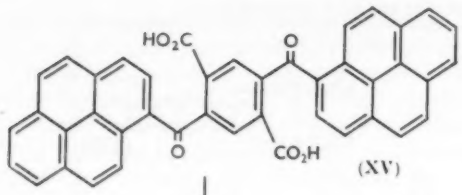
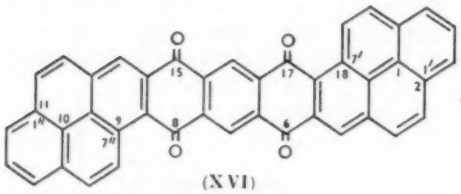


(XV)



(XVI)

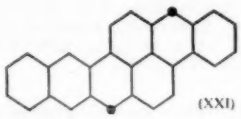
→ (XVII) → (XVIII) → (XIX)

(See Fig. 4)

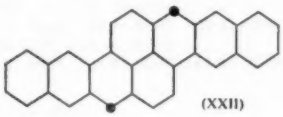
The differences between acenes and pyrenes are best illustrated by the following comparison of centrosymmetric annellated pyrenes and naphtho-acenes.

The pyrenes (XX, XXI, XXII) form pyrenequinones, on oxidation, in the positions marked with dots. The differences (4·79, 4·67, and 4·07) in $\sqrt{Å}$ in this annellation series

(XX)

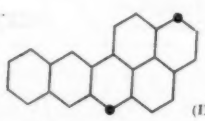


(XXI)

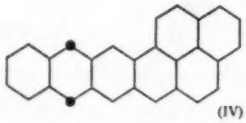


(XXII)

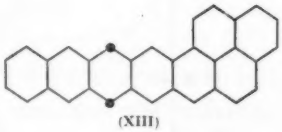
Wavelength of 1st band (Å) in benzene (log ε in parentheses)	4510 (4·60)		5160 (4·15)		5760 (4·45)
		4·79		+ 4·67		+ 4·07	
$\sqrt{Å}$		→ 67·16		→ 71·83		→ 75·90



(IX)



(IV)



(XIII)

Wavelength of 1st band (Å) in benzene (log ε in parentheses)	4580 (4·42)		5410 (4·15)		6330 (4·02)
		5·31		+ 5·87		+ 6·01	
$\sqrt{Å}$		→ 67·68		→ 73·55		→ 79·56

(beginning with 3 : 4-benzopyrene) are much smaller than in the acene series [5] (7·7 $\sqrt{Å}$) and not constant but decreasing. Contrary to this, the differences in the naphtho-acene series (IX, IV, XIII) are much larger and increasing (5·31, 5·87, and 6·01 $\sqrt{Å}$). If this series were extended the differences might well increase to the value 7·7 $\sqrt{Å}$ which is typical of the acene series.[5]

The high intensity (log ε 4·42) of the first band and the fact that oxidation of naphthopyrene (IX) gives a mixture of quinones [6] indicates that it still has pyrene character. The absorption spectrum of the closely related hydrocarbon (VII) (Fig. 2), however, shows a

[5] Clar, "Aromatische Kohlenwasserstoffe," Springer-Verlag, Berlin, 1952, p. 27.
[6] Cook and Hewett, *J.*, 1933, 403.

second group of bands (4350, 4100 Å) superimposed on the *para*-bands, which originates from another transition, probably to an excited acenoid structure.

The wavelength of the first *p*-bands of the later naphtho-acenes (IV and XIII) deviate more and more from the corresponding pyrenes (XXI and XXII) and their intensities decrease to the value (log ε about 4) which is characteristic for acenes. The reactivity, in particular the addition of maleic anhydride, and the ease of photo-oxidation in the marked positions increase with increasing acene character.

Experimental

M. p.s were taken in evacuated capillaries and corrected. Microanalyses are by Mr. J. M. L. Cameron and Miss M. W. Christie.

3-(3-*Carboxy*-2-*naphthoyl*)*pyrene* (I).—Naphthalene-2 : 3-dicarboxylic anhydride (2·0 g.) and aluminium chloride (2·5 g.) were mixed and added to tetrachloroethane (12 ml.). Powdered pyrene (2·5 g.) was then added, causing a violet-red coloration and a vigorous reaction, with complete dissolution. The solution was kept at 40° for 2 hr., then the complex was decomposed with dilute hydrochloric acid. The tetrachloroethane was distilled with steam, leaving pale yellow crystals which were filtered off and washed with benzene to remove excess of pyrene. The *acid* (4·0 g.; theor., 4·04 g.) crystallised from acetic acid as buff-coloured prisms, m. p. 259—260° (Found : C, 84·3; H, 4·3. $C_{28}H_{16}O_3$ requires C, 84·0; H, 4·0%). The colour in concentrated sulphuric acid changed from red, violet, blue to green-blue.

Naphtho(1′ : 7′-2 : 14)*pentacene*-6 : 13-*quinone* (II).—3-(3-Carboxy-2-naphthoyl)pyrene (1 g.) was dissolved by heat in benzoyl chloride (1 ml.) and α-chloronaphthalene (3 ml.). The solution was boiled for 35 min., cooled, and filtered. The *quinone* (0·85 g.) was washed with benzene, then recrystallised from nitrobenzene as orange plates, m. p. 340—341° (Found : C, 87·7; H, 4·1. $C_{28}H_{14}O_2$ requires C, 87·9; H, 3·7%). The colour in cold concentrated sulphuric acid was leaf-green. No vat could be obtained.

6 : 13(+7 : 12)-*Dihydronaphtho*(1′ : 7′-2 : 14)*pentacene* (III and III*A*).—The foregoing quinone (0·7 g.) was dissolved in pyridine (9 ml.), and zinc dust (4 g.) was added. The mixture was refluxed, and acetic acid (10 ml.) added during 4½ hr. The colour change in solution was orange, brown, cherry-red, and yellow. The solution was poured into hydrochloric acid, and the pink precipitate washed, finally with dilute aqueous ammonia, and dried. The pale pink powder (650 mg.) was distilled *in vacuo*, yielding a pink glass (0·5 g.). The red colour was due to a small amount of (IV) which was removed by chromatography in benzene–light petroleum on alumina. The *dihydronaphthopentacene* was obtained as very pale yellow, feathery crystals (400 mg.), m. p. 238—240°, by crytallisation from light petroleum (Found : C, 94·7; H, 5·0. $C_{28}H_{18}$ requires C, 94·9; H, 5·1%).

Naphtho(1′ : 7′-2 : 14)*pentacene* (IV).—The dihydro-compound (150 mg.) was sublimed at 300°/0·01 mm. over palladium–charcoal, giving red crystals (135 mg.), m. p. 348—350°, of the aromatic *hydrocarbon* (Found : C, 95·5; H, 4·7. $C_{28}H_{16}$ requires C, 95·4; H, 4·6%). The colour in cold concentrated sulphuric acid changed from blue, violet, green, brown to red-brown.

Maleic Anhydride Adduct of (IV).—The preceding naphthopentacene (50 mg.) was heated with maleic anhydride (100 mg.) and xylene (2 ml.). After a few minutes a clear yellow solution was obtained which deposited the *adduct*, yellow prisms, on cooling. These were filtered off, washed with xylene, and dried at 200° *in vacuo*. They decomposed above 220° (Found : C, 85·8; H, 3·8. $C_{32}H_{18}O_3$ requires C, 85·3; H, 4·0%).

3-(5 : 6 : 7 : 8-*Tetrahydro*-3-*methyl*-2-*naphthoyl*)*pyrene* (VI).—Pyrene-3-carboxyl chloride [7] (5·1 g.) and aluminium chloride (6 g.) were powdered together and added to methylene chloride (100 ml.). 6-Methyltetralin (3·65 g.) was added and the orange solution was refluxed for 2 hr. The complex was decomposed with dilute hydrochloric acid, and the methylene chloride distilled off, leaving a gum. This was treated successively with dilute hydrochloric acid, water, and dilute sodium hydroxide solution, whereupon the gum hardened. It was then filtered off, washed, and dried *in vacuo* (4·9 g.; theor., 7·48 g.). The product could not be obtained crystalline.

Naphtho(1′ : 7′-2 : 14)*pentacene* (IV) *and* 7 : 8-*Benzonaphtho*(1′ : 7′-2 : 12)*tetracene* (VII).—The above product was heated to 390° during 10 min. and copper bronze (*ca.* 0·5 g.) was added.

[7] Vollmann, Becker, Corell, and Streeck, *Annalen*, 1937, **531**, 110.

During the next 15 min. the temperature was raised to 410°, steam and hydrogen being evolved. The melt, on cooling, solidified to a black glass which was powdered and sublimed at 300°/0·01 mm. The semicrystalline sublimate (*ca.* 1 g.) was crystallised from benzene, then chromatographed in benzene–light petroleum on alumina in an inert atmosphere. The naphthopentacene (IV) was obtained as red leaflets, m. p. 348—350°, and the benzonaphthotetracene (VII) (*ca.* 50 mg.) as deep yellow leaflets, m. p. 332—333°.

3-(2-*Methyl*-1-*naphthoyl*)*pyrene* (VIII).—Pyrene-3-carboxyl chloride [7] (14 g.) and aluminium chloride (15 g.) were ground together and added to dry nitrobenzene (150 ml.). 2-Methylnaphthalene (8·75 g.) was added in a little nitrobenzene. The mixture, which had developed a purple colour, was stirred at 60—70° for 2 hr. The complex was decomposed with dilute hydrochloric acid, and the nitrobenzene layer washed with warm dilute hydrochloric acid, then with water. Steam-distillation gave a semisolid residue which was dissolved in benzene and extracted with warm dilute alkali. Pyrenecarboxylic acid (6·7 g.) was recovered by acidification of the alkaline extracts. The benzene was distilled off and the gummy residue (8·7 g.) recrystallised from alcohol, then from benzene, giving the *ketone* as yellow prisms, m. p. 194—195° (Found: C, 90·9; H, 4·6. $C_{28}H_{18}O$ requires C, 90·8; H, 4·9%).

7 : 8-*Benzonaphtho*(1′ : 7′-2 : 12)*tetracene* (VII).—The preceding ketone (6·7 g.) was heated to 390°, then the temperature was allowed to rise to 410° during 15 min. The almost quiescent melt was cooled and heated in a sublimation apparatus at 300°/0·01 mm. An orange glass was obtained which crystallised when treated with benzene. Chromatography in benzene–light petroleum gave, first, an oil and then the hydrocarbon (500 mg.), which recrystallised from benzene as yellow leaflets, m. p. (and mixed m. p. with product from earlier synthesis) 332—333° (Found: C, 95·3; H, 4·6. $C_{28}H_{16}$ requires C, 95·4; H, 4·6%).

3-(*Pyrene*-3-*carbonyl*)*anthraquinone*-2-*carboxylic Acid* (X).—Anthraquinone-2 : 3-dicarboxylic anhydride (22·4 g.) was ground with aluminium chloride (22·5 g.) and suspended in nitrobenzene (600 ml.) at 55°. Pyrene (20 g.) was added and the mixture was stirred at this temperature for 3½ hr., then treated with water (500 ml.) and concentrated hydrochloric acid (150 ml.). Steam-distillation removed the nitrobenzene, and the solid product was filtered off, extracted with dilute hydrochloric acid, washed with water, dried, and washed with benzene to remove excess of pyrene from the brownish-yellow powder (34 g.). Extraction with boiling ammonia solution and acidification of the extracts yielded the pure *acid* as a yellow precipitate, which crystallised from acetic acid as orange needles, m. p. 317—319° (Found: C, 79·7; H, 3·5. $C_{32}H_{16}O_5$ requires C, 80·0; H, 3·4%). The colour in concentrated sulphuric acid changed from red violet to violet and blue.

Naphtho(1′ : 7′-2 : 16)*hexacene*-6 : 15-8 : 13-*diquinone* (XI).—The *recrystallised* acid (1·7 g.) was dissolved in boiling benzoyl chloride (40 ml.) to give an orange solution, rapidly becoming brown. Addition of a trace of zinc chloride quickly changed the colour to blue-green and then to brown and deep red. The solution was cooled and allowed to crystallise. The deep red-maroon *diquinone* (1·15 g.) was filtered off, washed with benzoyl chloride, acetic acid, and ether, and recrystallised from nitrobenzene as red-maroon leaflets, m. p. 418—419° (Found: C, 82·8; H, 3·2. $C_{32}H_{14}O_4$ requires C, 83·1; H, 3·0%). With alkaline sodium dithionite it formed a two-stage vat, first a greenish-brown, then a reddish-brown one. The colour in cold concentrated sulphuric acid was green.

8 : 13(+7 : 14)-*Dihydronaphtho*(1′ : 7′-2 : 16)*hexacene* (XII and XII*A*).—The diquinone (1·6 g.) was dissolved in pyridine (160 ml.), zinc dust (10 g.) added, and the mixture refluxed while 80% acetic acid was added dropwise. The initial deep red colour of the solution changed quickly to blue-green, then back to pale red, and finally to canary-yellow. The mixture was refluxed for 17 hr. while a total of 90 ml. of acetic acid was added, then poured into much dilute hydrochloric acid, and the precipitated, incompletely reduced material (1·4 g.) washed, dried, and further reduced in 70 ml. of pyridine, with 30 ml. of acetic acid, for 11 hr. The solution was again poured into hydrochloric acid and the precipitate filtered off, washed, and dried (1·3 g.). The product was extracted with boiling xylene and repeated crystallisation of the extracted material gave the *dihydro-compound* (250 mg.) as yellow needles, m. p. 314—316° (Found: C, 95·0; H, 4·9. $C_{32}H_{20}$ requires C, 95·0; H, 5·0%).

Naphtho(1′ : 7′-2 : 16)*hexacene* (XIII).—The preceding dihydro-compound (100 mg.) was sublimed at 300°/0·01 mm. into closely-packed lumps of palladium–charcoal. The green deposit of naphthohexacene was sublimed from the charcoal at 350°. Extraction with boiling xylene removed unchanged dihydro-compound. Resublimation of the *hydrocarbon* gave

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clusters of blue-green leaflets (70 mg.), m. p. 384—386° (Found: C, 95·5; H, 4·4. $C_{32}H_{18}$ requires C, 95·5; H, 4·5%). The colour in cold concentrated sulphuric acid changed from violet to brown and green.

The *maleic anhydride adduct* was obtained by dissolving the naphthohexacene in molten maleic anhydride. Dilution of the melt with xylene and recrystallisation of the precipitate from xylene yielded yellow needles, decomp. >200° (Found: C, 85·0; H, 3·7. $C_{36}H_{20}O_3$ requires C, 86·4; H, 4·0%).

2 : 5-*Di*(*pyrene*-3-*carbonyl*)*terephthalic Acid* (XV).—Pyromellitic anhydride (9·7 g.) and anhydrous aluminium chloride (30 g.) were ground together and added at room temperature to a stirred solution of pyrene (25 g.) in benzene (80 ml.). On gentle heating, exothermic reaction occurred. After being kept at room temperature for 2 days the complex was decomposed with dilute hydrochloric acid. The benzene was boiled off and the solid product was filtered off and washed with dilute hydrochloric acid, then with water. The *acid* was extracted from the crude product as its sparingly soluble ammonium salt from which it was obtained by acidification (12·5 g.). It recrystallised from acetic acid in yellow needles, m. p. 334—336° (Found: C, 80·0; H, 3·5. $C_{42}H_{22}O_6$ requires C, 81·0; H, 3·5%). The colour in sulphuric acid was violet red.

Dinaphtho(1′ : 7′-2 : 18)(7″ : 1″-9 : 11)*heptacene*-6 : 17-8 : 15-*diquinone* (XVI).—The acid (3 g.) was dissolved in boiling benzoyl chloride (45 ml.) containing a trace of zinc chloride. The solution developed a greenish-yellow colour which changed to violet-red. After the solution had been refluxed for 15 min. the *quinone* began to crystallise. It was filtered off, washed with benzoyl chloride, acetic acid, and ether (yield 0·7 g.), and sublimed *in vacuo* (0·005 mm.) at 420° in violet-red plates, m. p. 500—502° (Found: C, 85·8; H, 3·4. $C_{42}H_{18}O_4$ requires C, 86·0; H, 3·1%).

8 : 15(+7 : 16)-*Dihydrodinaphtho*(1′ : 7′-2 : 18)(7″ : 1″-9 : 10)*heptacene* (XVII).—The preceding diquinone (1 g.) was powdered with zinc dust (10 g.) and added to pyridine (40 ml.). Acetic acid (80%; 50 ml.) was added to the refluxing mixture during 15 hr., and the amount of zinc was renewed twice. The colour of the solution changed from violet-brown to yellow-brown, then to yellow. The supernatant hot pyridine solution was poured into water (200 ml.). The yellow precipitate was filtered off, washed with hot dilute hydrochloric acid, then with water, and dried (780 mg.). The zinc residues were dissolved in concentrated hydrochloric acid. The diluted solution was filtered and the residue washed with water and dried (yield, 115 mg. of pale yellow-brown material). The combined product was extracted with boiling xylene (2 × 50 ml.) (residue: 660 mg.), the xylene solution evaporated to dryness, and the residue sublimed at 360°/0·01 mm. It gave a yellow crystalline sublimate which, when recrystallised from xylene, yielded the *dihydro-compound* as yellow-brown needles (120 mg.), m. p. 413—414° (Found: C, 95·2; H, 4·5. $C_{42}H_{24}$ requires C, 95·4; H, 4·6%).

Dinaphtho(1′ : 7′-2 : 18)(7″ : 1″-9 : 11)-*heptacene* (XVIII).—The preceding compound (50 mg.) was sublimed into closely-packed palladium–charcoal lumps at 375°/0·001 mm. during several hours. The temperature was raised to 415° and after about 16 hr. 25 mg. of the aromatic *hydrocarbon* had sublimed as deep green-black needles, m. p. 461—462°. It dissolved very slowly in concentrated sulphuric acid with a brown violet colour (Found: C, 95·7; H, 4·3. $C_{42}H_{22}$ requires C, 95·8; H, 4·2%).

The *maleic anhydride adduct* crystallised from a solution of dinaphthoheptacene in molten maleic anhydride when the melt was diluted with xylene. Recrystallised from xylene it formed yellowish prisms, decomp. >200° (Found: C, 88·8; H, 3·7. $C_{46}H_{24}O_3$ requires C, 88·4; H, 3·9).

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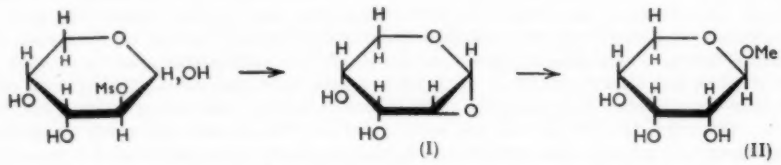
520. *The Action of Base on Methanesulphonyl Esters of Reducing Sugars.*

By D. C. C. Smith.

Reaction of 4-*O*-formyl-2-*O*-methanesulphonyl-D-arabinose with sodium methoxide gives rise to a mixture of methyl pentosides. 3 : 5-*O*-Benzylidene-4-*O*-formyl-2-*O*-methanesulphonyl-*aldehydo*-D-arabinose hydrate, 1 : 4 : 6-tri-*O*-acetyl-3-*O*-methanesulphonyl-2-*O*-methyl-α-D-glucose, 3-*O*-methanesulphonyl-D-xylose, and 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose have been synthesised. Alkaline hydrolysis of each of these substances conforms to the patterns already described for 4-*O*-formyl-2-*O*-methanesulphonyl-D-arabinose and 3-*O*-methanesulphonyl-D-glucose.[1]

ALKALINE hydrolysis of 2-*O*-methanesulphonyl-D-arabinose is reported to give D-ribose in high yield, accompanied by a small amount of D-arabinose.[2] Hydrolysis of 4-*O*-formyl-2-*O*-methanesulphonyl-D-arabinose[3] with precautions against exposure of the products unnecessarily to alkali, gives D-ribose containing no D-arabinose.[1] Alkaline hydrolysis of 2-*O*-methanesulphonyl-D-arabinose has been followed titrimetrically and found to be sixteen times faster than that of methyl 2-*O*-methanesulphonyl-(αβ)-D-arabinopyranoside under the same conditions, suggesting that the free reducing group plays an important part in the reaction. Anhydro-ring formation involving the reducing group (cf. I), followed by opening of the anhydro-ring by attack of hydroxyl ion at the anomeric carbon, has been suggested.[2]

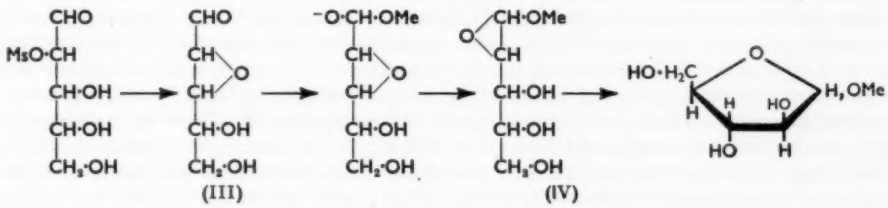


In order to test this mechanism, sodium methoxide has been substituted for sodium hydroxide. The reaction was followed titrimetrically and found to be twenty times slower than that with aqueous sodium hydroxide of equivalent concentration. The main product was a mixture of methyl pentosides with free arabinose and ribose. The last two products were probably produced by traces of the more reactive sodium hydroxide. Using 4-*O*-formyl-2-*O*-methanesulphonyl-D-arabinose in place of 2-*O*-methanesulphonyl-D-arabinose gave a 97% yield of methyl pentosides uncontaminated with reducing sugars; this is probably because saponification of the formyl ester grouping removes traces of hydroxyl ions that are present and so prevents them from reacting at the anomeric position. Methyl β-D-ribopyranoside was isolated from the mixture and the combined results of periodate oxidation, hydrolysis, measurements of optical rotation, and paper chromatography indicate the presence in the reaction product of 62% of this substance accompanied by both anomeric methyl D-arabinofuranosides. The presence of only methyl pentosides in the product indicates that methanol or methoxide ions must attack the anomeric position at some stage. Such a reaction has already been described in the conversion of 2 : 3-*O*-*iso*propylidene-5-*O*-toluene-*p*-sulphonyl-L-rhamnose into methyl 2 : 3-*O*-*iso*propylidene-β-D-allomethyloside,[4] and, since this work was completed, in the conversion of

[1] D. C. C. Smith, *Chem. and Ind.*, 1955, 92.
[2] Jones and Nicholson, *J.*, 1955, 3050.
[3] Barker and D. C. C. Smith, *Chem. and Ind.*, 1952, 1035.
[4] Levene and Compton, *J. Biol. Chem.*, 1936, **116**, 169.

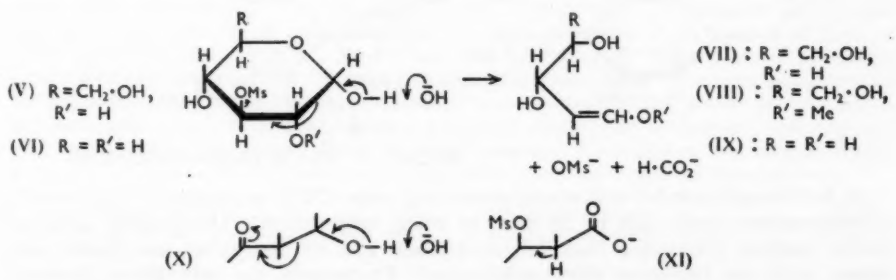
1 : 3 : 5-tri-*O*-benzoyl-2-*O*-methanesulphonyl-α-D-ribose into methyl α-D-arabinopyranoside.[5]

In the present case, the intermediate formation of 1 : 2-anhydro-D-ribopyranose (I) would enable attack of methoxide ion to occur at the anomeric position, and can account for the predominance of β-anomers, and particularly of methyl β-D-ribopyranoside (II), in the product. The formation of methyl D-arabinosides from 2-*O*-methanesulphonyl-D-arabinose involves retention of configuration at position 2. In view of the mild reaction conditions and since inversion of configuration with intramolecular nucleophilic assistance always accompanies such mild alkaline hydrolysis of sulphonyl esters, it seems probable that the formation of methyl arabinosides in this reaction involves two successive inversions at position 2. This can occur by the intermediate formation of 2 : 3-anhydro-D-ribose (III), subsequent addition of methoxide ion in two possible stereo-configurations to



the 1-carbonyl group, and migration of the epoxide ring to give two anomeric methyl epoxy-ethers (IV). Such substances would be expected [6] to react with alcoholic sodium alkoxide at room temperature. The oxygen on position 4 is in a favourable situation to act as the attacking alkoxide ion and in so doing would give rise to an anomeric mixture of methyl D-arabinofuranosides.

The reaction of 3-*O*-methanesulphonyl-D-glucose with sodium hydroxide, described in a preliminary communication, has been found to yield 2-deoxy-D-ribose and formate. The mechanism proposed [1] (V) involves the enol of 2-deoxy-D-ribose (VII) as an intermediate. This elimination has an analogy in the reverse aldol reaction (X), the two



having the relation proposed by Hughes [7] as existing between a removable group X in C—X and the —*M* effect of oxygen in C=O. The related system (XI) has been found by Linstead, Owen, and Webb [8] to undergo a different type of elimination, leaving an unsaturated acid as the main product. This reaction is slower than the eliminations reported in the present work and probably takes place instead because of the —*M* effect of the

[5] Ness and Fletcher, *J. Amer. Chem. Soc.*, 1956, **78**, 4710.
[6] Stevens and Dykstra, *ibid.*, 1954, **76**, 4402.
[7] Hughes, *Nature*, 1941, **147**, 812.
[8] Linstead, Owen, and Webb, *J.*, 1953, 1211.

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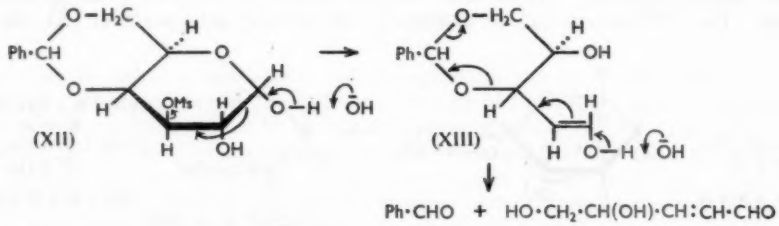
potential carbonyl group of the carboxylic acid group diverts any tendency for the carboxylate anion to supply electrons in assisting elimination of the methanesulphonyloxy-group. The elimination of the phosphate group employed in stepwise degradation of oligonucleotides [9] is more likely to be analogous to (V), yielding formic acid: this would explain its rapidity and also the neutralisation of two equivalents of alkali per nucleotide residue.[9]

Evidence for the intermediate formation of the enol (VII) in the reaction of 3-*O*-methanesulphonyl-D-glucose with sodium hydroxide has been obtained from the reaction of 1 : 4 : 6-tri-*O*-acetyl-3-*O*-methanesulphonyl-2-*O*-methyl-α-D-glucopyranose with sodium hydroxide. The tri-*O*-acetyl derivative was used for this reaction rather than free 3-*O*-methanesulphonyl-2-*O*-methyl-D-glucose because the glycosidic grouping in methyl 4 : 6-benzylidene-3-*O*-methanesulphonyl-2-*O*-methyl-β-D-glucopyranoside was found to be resistant to acid hydrolysis, an effect frequently reported for various toluene-*p*-sulphonyl esters of methyl glycosides.[2] However, acetolysis of our methyl glycoside occurred smoothly at room temperature. Quantitative saponification of the resulting 1 : 4 : 6-tri-*O*-acetyl-3-*O*-methanesulphonyl-2-*O*-methyl-α-D-glucopyranose consumed 4·8 equivalents of alkali, yielding formate (detected chromatographically) and substances stable to excess of alkali and giving a strong Dische reaction.[10] These were isolated as a syrup showing a strong absorption band at 1685 cm.$^{-1}$, consistently with the double-bond stretching vibration of an enol ether [11] but whose methoxyl content was too low for the expected 5-methoxypent-4-ene-1 : 2 : 3-triol (VIII), and which on drying was transformed into a glass with loss of methanol. This behaviour resembles that of the polymer formed from methyl 2-deoxy-D-ribofuranoside by loss of methanol,[12] and it seems likely that, though it could not be isolated, the triol (VIII) is the initial product of saponification.

3-*O*-Methanesulphonyl-D-xylose (VI) was synthesised from 3-*O*-methanesulphonyl-1 : 2-5 : 6-di-*O*-*iso*propylidene-D-glucose and found to react with sodium hydroxide in an analogous manner. When precautions were taken to avoid excess of alkali, formate (detected chromatographically) and D(−)-βγ-dihydroxybutyraldehyde (keto-form of IX) were obtained.



4 : 6-*O*-Benzylidene-3-*O*-methanesulphonyl-D-glucose (XII) neutralised 3 equivalents of 0·01N-sodium hydroxide in 20 min. at room temperature. The product gave no Dische reaction, confirming that 2-deoxy-D-ribose and its derivatives are absent, and benzoic acid was recovered after acidification. Presumably the benzylidene group is eliminated from the enol (XIII) initially formed giving benzaldehyde which becomes oxidised in dilute aqueous solution to benzoic acid with neutralisation of a further equivalent of alkali. This accords with the mechanism for elimination of alkoxy-groups from β-alkoxycarbonyl compounds involving initial enolisation suggested by Corbett and Kenner.[13] Formation of the requisite enol by elimination of the methanesulphonyl group occurs much more rapidly than formation of a similar enol by keto–enol tautomeric change.

[9] Brown, Fried, and Todd, *J.*, 1955, 2206.
[10] Deriaz, Stacey, Teece, and Wiggins, *J.*, 1949, 1222.
[11] Meakins, *J.*, 1953, 4170.
[12] Overend, Shafizadeh, and Stacey, *J.*, 1951, 994.
[13] Corbett and Kenner, *J.*, 1953, 2245.

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Hence the elimination of the benzylidene group in 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose occurs more rapidly than the reported [14] elimination of the *iso*propylidene group and benzylidene group from 2 : 3-5 : 6-di-*O*-*iso*propylidene-D-mannose and 4 : 6-*O*-benzylidene-D-glucose respectively.

Oxidation of 4:6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose with sodium periodate yielded 3 : 5-*O*-benzylidene-4-*O*-formyl-2-*O*-methanesulphonyl-*aldehydo*-D-arabinose hydrate, which neutralised 3 equivalents of 0·01N-alkali within 5 minutes and a further equivalent during the next hour. With N-sodium hydroxide for 10 minutes the above compound gave benzaldehyde which was isolated as its 2 : 4-dinitrophenylhydrazone in 71% yield. The release of benzaldehyde is only slightly slower than from 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose, and the 3 : 5-*O*-benzylidene-D-ribose which is presumably initially formed apparently eliminates the benzylidene group to yield saccharinic acids, four of which were detected as their lactones by paper chromatography. The rapidity of the elimination of the benzylidene grouping as compared with previous examples of this reaction may be due to the *aldehydo*-structure of 3 : 5-*O*-benzylidene-D-ribose.

In the preparation of 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose by condensation of 3-*O*-methanesulphonyl-D-glucose with benzaldehyde, a di-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose was obtained as a by-product. Since 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose shows no tendency to condense further with benzaldehyde, this is probably 1 : 2-5 : 6-di-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucofuranose; it was reduced with lithium aluminium hydride to a hitherto unknown di-*O*-benzylideneglucose.

Experimental

Paper chromatograms were in the system butan-1-ol–water unless otherwise stated.

Reaction of 4-O-*Formyl*-2-O-*methanesulphonyl*-D-*arabinose with Sodium Methoxide.*—This compound (1·0 g.) was added to a solution prepared by dissolving sodium (0·5 g.) in dried methanol (100 c.c.). After 24 hr. at room temperature the colourless solution was diluted with chloroform (100 c.c.), neutralised with carbon dioxide, filtered, and evaporated. Extraction of the residue with chloroform gave methyl pentosides as a viscous syrup (0·36 g., 97%), subliming at 95° (bath-temp.)/10^{-5} mm., $[\alpha]_D^{18}$ −79·1° (*c* 1·2 in H_2O) (Found : C, 43·85; H, 7·35; OMe, 18·65. Calc. for $C_6H_{12}O_5$: C, 43·9; H, 7·4; OMe, 18·9%). It migrated as one main spot of R_F 0·41, and one or more unresolved and indistinct spots of R_F 0·22—0·41, detected with ammoniacal silver nitrate. No free pentoses were present. A portion was hydrolysed with 0·5N-hydrochloric acid at 95° for 1 hr., neutralised with silver carbonate, and examined by paper chromatography in butan-1-ol–water and in ethyl methyl ketone–water. Ribose and arabinose were both present, possibly a trace of xylose, and no lyxose. Spraying with acid naphtharesorcinol reagent failed to reveal ketoses. R_F values of the various methyl glycosides of ribose and arabinose in butanol–water were determined for comparison :

α-D-Ribopyranoside	0·29	α-D-Ribofuranoside	0·26
β-D-Ribopyranoside	0·41	β-D-Ribofuranoside	0·41
α-L-Arabopyranoside	0·22		
β-L-Arabopyranoside	0·26	(αβ)-L-Arabofuranosides	0·30

Only the methyl β-D-ribosides correspond in R_F to the main spot, R_F 0·41, of the mixture. The identity of this spot was shown by chromatographing the mixture (70 mg.) on a sheet of No. 1 Whatman paper 21″ wide, extracting the section at the leading edge of the component of R_F 0·41, and recrystallising the product from ethyl acetate; methyl β-D-ribopyranoside (15 mg.) obtained had m. p. and mixed m. p. 80—83°.

The product of the above vacuum-sublimation (79·26 mg.) and 0·1928M-sodium metaperiodate (7 c.c.) were made up to 25 c.c. and kept at room temperature. Excess of periodate was determined by Barnebey's method.[15] Free acid was determined after reduction of excess

[14] Corbett, Kenner, and Richards, *J.*, 1955, 1709.
[15] Barnebey, *J. Amer. Chem. Soc.*, 1916, **38**, 330.

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of periodate with ethylene glycol, by titrating aliquot parts with 0·01N-sodium hydroxide to the end-point of phenol-red :

Time (min.)	4	12	30	60	90	130	180	1200
Periodate consumed (mols.)	0·96	1·06	1·27	1·35	1·49	1·57	1·64	1·64
Time (min.)	6	14	45	90	130	180	1200	
Acid released (equiv.)	0·41	0·41	0·46	0·46	0·51	0·55	0·62	

If the release of 0·62 equiv. of acid is due to the oxidation of 0·62 mol. of methyl pentopyranoside then $2 \times 0{\cdot}62 = 1{\cdot}24$ mols. of periodate will be consumed in this. The remaining slow consumption of periodate (1·64—1·24 = 0·40 mol.) agrees closely with the unaccounted methyl pentoside (1·00—0·62 = 0·38 mol.), suggesting that this consists mostly of slowly oxidised methyl arabinofuranoside. The observed rotation of the methyl pentoside is consistent with the composition : methyl β-D-ribopyranoside ($[\alpha]_D$ −106·5°) (61%), α-D-arabinofuranoside ($[\alpha]_D$ +123°) (9%), and β-D-arabinofuranoside ($[\alpha]_D$ −86°, calculated by applying Hudson's isorotation rules to the foregoing value) (30%).

The specific rotation of the products after completion of the oxidation was $[\alpha]_D^{18}$ −81·4° (calc. as $C_6H_{12}O_5$; *c* 0·317) when compared with the values given by Jackson and Hudson,[16] for the optical rotations of the periodate oxidation products of methyl pentosides of the D-series, recalculated as referring to the specific rotations of $C_6H_{12}O_5$: α-furanoside, +119° ; α-pyranoside, +99° ; β-furanoside, −149° ; β-pyranoside, −99°. This indicates a predominance of β-anomers in the glycosidic mixture. The observed rotation of the oxidation products (−81·4°) is consistent with the composition : methyl β-D-ribopyranoside (61%), α-D-arabinofuranoside (14%), and β-D-arabinofuranoside (25%).

Methyl 4 : 6-O-*Benzylidene*-3-O-*methanesulphonyl*-2-O-*methyl*-β-D-*glucopyranoside and its Anomer.*—3-*O*-Methanesulphonyl-D-glucose[17] (10 g.) in 2% methanolic hydrogen chloride (300 c.c.) was refluxed for 20 hr., neutralised with silver oxide (30 g.), filtered through active charcoal, and evaporated to a syrup (10·8 g.). This was shaken with benzaldehyde (150 c.c.) and powdered anhydrous zinc chloride (30 g.) for 12 hr. Shaking the clear solution with light petroleum and water precipitated a gum which solidified. This was powdered, washed with light petroleum and water, and dried (product A) (10·5 g.). This was methylated with silver oxide and methyl iodide (nine treatments), isolated with chloroform, and chromatographed on neutral alumina. Benzene eluted *methyl* 4 : 6-O-*benzylidene*-3-O-*methanesulphonyl*-2-O-*methyl*-β-D-*glucopyranoside*, prisms (from ethyl acetate–light petroleum) (3·4 g.), m. p. 109—110°, $[\alpha]_D^{20}$ −66° (*c* 1·7 in $CHCl_3$) (Found : C, 51·5; H, 5·7. $C_{16}H_{22}O_8S$ requires C, 51·4; H, 5·9%). Ether eluted *methyl* 4 : 6-O-*benzylidene*-3-O-*methanesulphonyl*-α-D-*glucopyranoside*, prisms (from chloroform–ether) (2·7 g.), m. p. 146—147°, $[\alpha]_D^{20}$ +94·4° (*c* 1·0 in $CHCl_3$) (Found : C, 49·7; H, 5·6. $C_{15}H_{20}O_8S$ requires C, 50·0; H, 5·6%).

In a separate experiment the product (A) was extracted exhaustively with ether to remove the α-glycoside, and the residue crystallised from chloroform–methanol to yield *methyl* 4 : 6-O-*benzylidene*-3-O-*methanesulphonyl*-β-D-*glucopyranoside* (1·65 g.), prisms (from chloroform–methanol), m. p. 187—188°, $[\alpha]_D^{20}$ −52·5° (*c* 2·9 in $CHCl_3$) (Found : C, 49·7; H, 5·7%).

Methylation of methyl 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-α-D-glucopyranoside (1·85 g.) with methyl iodide, methanol, and silver oxide (nine treatments), followed by chromatography on neutral alumina in benzene, yielded *methyl* 4 : 6-O-*benzylidene*-3-O-*methanesulphonyl*-2-O-*methyl*-α-D-*glucopyranoside* (1·26 g.) as plates (from ethyl acetate–light petroleum, m. p. 163—164°, $[\alpha]_D^{20}$ +71·8° (*c* 2·1 in $CHCl_3$) (Found : C, 51·4; H, 5·8%).

1 : 4 : 6-*Tri*-O-*acetyl*-3-O-*methanesulphonyl*-2-O-*methyl*-α-D-*glucopyranose.*—Methyl 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-2-*O*-methyl-β-D-glucopyranoside (2·9 g.) was dissolved in a cooled mixture of acetic anhydride (70 c.c.), acetic acid (30 c.c.) and concentrated sulphuric acid (2 c.c.). The reaction, followed polarimetrically, was completed in 2 hr. at room temperature. The mixture was poured into a solution of sodium acetate trihydrate (150 g.) in the minimum volume of water, and after 45 min. the milky suspension was extracted with ether. The extract was dried (Na_2SO_4), and ether and acetic acid distilled off to leave a colourless syrup (3·9 g.) containing, besides the product, benzylidene acetate. Dissolution in ethyl acetate–light petroleum, followed by intense cooling, initiated crystallisation. Repeated

[16] Jackson and Hudson, *J. Amer. Chem. Soc.*, 1937, **59**, 994.
[17] Helferich, Dressler, and Griebel, *J. prakt. Chem.*, 1939, **153**, 285.

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recrystallisation from these solvents yielded 1 : 4 : 6-*tri*-O-*acetyl*-3-O-*methanesulphonyl*-2-O-*methyl*-α-D-*glucopyranose* (0·60 g.), m. p. 114—115°, $[\alpha]_D^{20}$ +104·2° (*c* 1·6 in $CHCl_3$) (Found: C, 42·5; H, 6·0. $C_{12}H_{22}O_{11}S$ requires C, 42·2; H, 5·6%).

Reaction of 1 : 4 : 6-*Tri*-O-*acetyl*-3-O-*methanesulphonyl*-2-O-*methyl*-α-D-*glucopyranose with Sodium Hydroxide.*—This substance (0·0420 g.) in methanol (1 c.c.) was treated with 0·00924N-sodium hydroxide (80 c.c.) and made up to 100 c.c. with water. The amount of sodium hydroxide neutralised was determined by titration of aliquot parts with 0·01N-sulphuric acid to the end-point of phenol-red:

Time (min.)	5	15	40	95	180	1200
Alkali neutralised (equiv./mol.)	1·7	2·8	3·7	4·3	4·5	4·8

Paper chromatography of the solution showed sodium formate (R_F 0·04; strongly reducing to ammoniacal silver nitrate) and a substance described below (R_F 0·45).

A mixture of 1 : 4 : 6-tri-*O*-acetyl-3-*O*-methanesulphonyl-2-*O*-methyl-α-D-glucopyranose with benzylidene acetate (2·96 g., estimated to contain 1·8 g. of the sugar derivative) in methanol (10 c.c.) was mixed with N-sodium hydroxide (60 c.c.) and immediately evaporated *in vacuo*. The residue in methanol (30 c.c.) and chloroform (200 c.c.) was neutralised with carbon dioxide, filtered to remove insoluble salts, evaporated *in vacuo*, extracted with chloroform, filtered, and again evaporated to a clear syrup (0·73 g.). It showed a strong absorption band at 1685 $cm.^{-1}$, attributable to an enol ether,[11] but paper chromatography revealed three components, with R_F's zero (tailing forward), 0·45, and 0·54 respectively, all giving a mauve colour when sprayed with Dische reagent (diphenylamine sulphate) (0·1 g.) and sulphuric acid (one drop) in glacial acetic acid (50 c.c.) and then heated at 80°. Chromatograms of freshly saponified 1 : 4 : 6-tri-*O*-acetyl-3-*O*-methanesulphonyl-2-*O*-methyl-α-D-glucopyranose occasionally showed only the component of R_F 0·45, making it probable that this is the initial product, but the other components appeared spontaneously on storage. The syrup as isolated had $[\alpha]_D^{20}$ −18·3° (*c* 3·5 in MeOH) (Found: C, 46·1; H, 7·6; OMe, 7·2%). When dried to constant weight *in vacuo* at 25° it set to a hard glass, $[\alpha]_D^{20}$ zero (*c* 2·0 in MeOH), showing only the component of R_F zero (Found: C, 52·6, 52·6, 50·8; H, 6·7, 6·2, 6·0; OMe, 1·9. Calc. for $C_8H_8O_8$: C, 51·7; H, 6·9; OMe, 0%).

1 : 2-O-iso*Propylidene*-3-O-*methanesulphonyl*-α-D-*xylofuranose.*—1 : 2-5 : 6-Di-*O*-*iso*propylidene-3-*O*-methanesulphonyl-D-glucose (38 g.) in acetic acid (60 c.c.) and water (20 c.c.) was heated at 50—60° for 3 hr., evaporated *in vacuo*, diluted with water (200 c.c.), made alkaline (40 c.c. of N-sodium hydroxide), kept for 2 hr., then brought to pH 5 (20 c.c. of N-sulphuric acid). This solution, stirred in ice, was treated with powdered sodium metaperiodate (52 g.) at such a rate as to keep the temperature below 20°. The pasty suspension was kept for 1 hr. at room temperature, and the solids were filtered off and washed with methanol (100 c.c.). The aqueous filtrate and the methanol washings were combined and run slowly into a vigorously stirred suspension of anhydrous magnesium sulphate (500 g.) in ether (3 l.). The magnesium sulphate was filtered off and washed with ether. The combined filtrate and washings were evaporated to a syrup (30·7 g.) smelling of formaldehyde. This was taken up in methanol (180 c.c.) and water (60 c.c.) and treated with potassium borohydride (9·0 g.). The reaction was marked by a vigorous effervescence and was moderated by cooling. After 15 min. acetic acid was added to decompose excess of reducing agent, and methanol was distilled off *in vacuo*. The residue was diluted with water (250 c.c.) and extracted several times with chloroform. Evaporation of the chloroform extracts yielded a syrup (29·6 g.) which crystallised. This was taken up in ethyl acetate (100 c.c.), diluted with light petroleum (100 c.c.), and on being seeded deposited crystals of 1 : 2-O-iso*propylidene*-3-O-*methanesulphonyl*-α-D-*xylofuranose* (22·4 g.), m. p. 81—83°, $[\alpha]_D^{18}$ −26·1° (*c* 3·0 in $CHCl_3$) (Found: C, 40·25; H, 5·9. $C_9H_{16}O_7S$ requires C, 40·3; H, 6·0%).

3-O-*Methanesulphonyl*-D-*xylose.*—1 : 2-*O*-*iso*Propylidene-3-*O*-methanesulphonyl-α-D-xylofuranose (21·9 g.) in ethanol (50 c.c.) and water (50 c.c.) was heated with N-sulphuric acid (2 c.c.) for 3 hr. Ethanol and acetone were distilled off, water (50 c.c.) added, and the solution heated on a water-bath for 1 hr. The brown solution was filtered through Norit and passed successively through columns of Amberlite IR-120 (H^+) (100 g.) and Amberlite IR-4B (basic form) (100 g.). Evaporation of the eluate *in vacuo* was accompanied by spontaneous crystallisation. The residue was taken up in methanol (180 c.c.), seeded, and allowed to evaporate. 3-O-*Methanesulphonyl*-D-*xylose* was obtained (13·0 g.), having m. p. 140—141°, $[\alpha]_D^{24}$ +37·6° (15

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min.), +24·5° (33 min.), +20·5° (61 min.), +19·6° (114 min. and equil.) (*c* 3·7 in H_2O) (Found: C, 31·3; H, 5·2. $C_6H_{12}O_7S$ requires C, 31·5; H, 5·3%).

Reaction of 3-O-*Methanesulphonyl*-D-*xylose with Sodium Hydroxide.*—3-*O*-Methanesulphonyl-D-xylose (5·0 g.) in water (1 l.) was stirred, and N-sodium hydroxide (33 c.c., 75% of the theoretical amount) was run in continuously during 1·5 hr. The solution was passed through Amberlite IR-120 (H^+) (100 g.) and then through Amberlite IR-4B (basic form) (100 g.) and evaporated *in vacuo* to a syrup (2·3 g.). Paper chromatograms developed in water-saturated butan-1-ol and sprayed with ammoniacal silver nitrate showed the presence of 3-*O*-methanesulphonyl-D-xylose (R_F 0·31), D(−)-βγ-dihydroxybutyraldehyde (R_F 0·49), and unknown substances B (R_F 0·13) and C (R_F 0·10). The mixture was taken up in butan-1-ol (20 c.c.), saturated with water and run on a hydrocellulose column (5·5 cm. diam., 23 cm. long) and eluted with water-saturated butan-1-ol. The effluent from the column yielded successively D(−)-βγ-*dihydroxybutyraldehyde* (0·79 g.), mixture (0·21 g.), 3-*O*-methanesulphonyl-D-xylose (0·66 g.), B (0·30 g.), and C (0·04 g.). D(−)-βγ-Dihydroxybutyraldehyde was a colourless syrup, $[\alpha]_D^{20}$ −6·4° (immediate and equil. value) (*c* 1·2 in H_2O) (Found: C, 46·3; H, 7·4. $C_4H_8O_3$ requires: C, 46·1; H, 7·7%). B and C remain unidentified but they may be products of aldol self-condensation of D(−)-βγ-dihydroxybutyraldehyde.

Condensation of 3-O-*Methanesulphonyl*-D-*glucose with Benzaldehyde.*—3-*O*-Methanesulphonyl-D-glucose (5 g.) was shaken with benzaldehyde (70 c.c.) and powdered anhydrous zinc chloride (20 g.) for 12 hr. Shaking the product with light petroleum and water precipitated a gum which solidified. This was powdered, washed with light petroleum and water, and dried (product D) (5·6 g.). Recrystallisation from chloroform containing a few drops of methanol yielded 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose as its chloroform-adduct, plates, m. p. 126—128°, $[\alpha]_D^{19}$ +27·1° (*c* 1·88 in 1 : 1 $CHCl_3$–MeOH). This gave variable analyses (Found: C, 43·75, 39·8, 43·2; H, 4·7, 4·35, 4·9; Cl, 9·45, 6·95, 5·95%), illustrating that chloroform is partly removed on drying. Mother-liquor from this crystallisation when concentrated and diluted with methanol deposited *di*-O-*benzylidene*-3-O-*methanesulphonyl*-D-*glucose* (1·1 g.) as needles, m. p. 179—181°, $[\alpha]_D^{17}$ +84·2° (*c* 2·28 in $CHCl_3$) (Found: C, 57·8; H, 5·4. $C_{21}H_{22}O_8S$ requires C, 58·1; H, 5·1%).

A similar experiment using less zinc chloride (2·5 g.) yielded the chloroform adduct of the monobenzylidene compound (2·9 g.) and the di-*O*-benzylidene compound (0·5 g.).

Product D (1·23 g.) was chromatographed on neutral alumina: ethyl acetate (1 part) and chloroform (2 parts) eluted the di-*O*-benzylidene compound (0·49 g.); methanol eluted 4 : 6-O-*benzylidene*-3-O-*methanesulphonyl*-D-*glucose* (0·52 g.), needles (from ethyl acetate–light petroleum), m. p. 144—146°, $[\alpha]_D^{18}$ +32·8° (*c* 1·05 in 1 : 1 $CHCl_3$–MeOH) (Found: C, 48·5; H, 5·2. $C_{14}H_{18}O_8S$ requires C, 48·6; H, 5·2%).

Di-O-*benzylidene*-D-*glucose.*—Di-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose (0·3 g.) and lithium aluminium hydride (1·0 g.) were stirred in ether under reflux for 12 hr. Ethyl acetate, methanol, and water were added in this order, and the product was taken up in ether, washed with sodium hydroxide solution and water, dried, and evaporated to a residue (0·12 g.) which, recrystallised from ethyl acetate–light petroleum (yield, 0·09 g.), had m. p. 162—163°, $[\alpha]_D^{18}$ +123° (*c* 0·64 in $CHCl_3$) (Found: C, 67·15; H, 5·65. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·7%).

3 : 5-O-*Benzylidene*-4-O-*formyl*-2-O-*methanesulphonyl*-aldehydo-D-*arabinose Hydrate.*—The chloroform adduct of 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose (1·6 g.) was dissolved in water (30 c.c.) with warming. The resulting solution was cooled, stirred with powdered sodium metaperiodate (1·6 g.), and kept in darkness at 0° for 2 days. The needles which had separated were washed with cold water and air-dried (0·44 g.); they had m. p. 164—166°, $[\alpha]_D^{20}$ −4·22° (initial and equil.) (*c* 2·47 in 1 : 1 $CHCl_3$–MeOH) (Found: C, 46·35; H, 5·15. $C_{14}H_{16}O_8S,H_2O$ requires C, 46·4; H, 5·0%).

Methyl 2-O-*Methanesulphonyl*-(αβ)-D-*arabinopyranoside.*—4-*O*-Formyl-2-*O*-methanesulphonyl-D-arabinose[3] (0·75 g.) in 4% dry methanolic hydrogen chloride (80 c.c.) was heated under reflux for 6 hr., cooled, neutralised with silver carbonate, filtered through Norit, and evaporated to a colourless syrup (0·54 g.) (Found: C, 35·1; H, 6·05. Calc. for $C_7H_{14}O_7S$: C, 34·7; H, 5·8%).

Measurement of the Approximate Comparative Rates of Alkaline Hydrolysis (see Tables).—Each sugar or glucoside (0·25 millimol.) was dissolved in 0·01N-sodium hydroxide (50 c.c.) at room temperature; aliquot parts withdrawn at the stated times were titrated with 0·01N-sulphuric acid to the end-point of phenol-red.

2-*O*-Methanesulphonyl-D-arabinose :

Time (min.)	3	6	10	23	39
Alkali neutralised (equiv./mol.)	0·26	0·48	0·62	0·84	0·86

4-*O*-Formyl-2-*O*-methanesulphonyl-D-arabinose :

Time (min.)	5	9	20	32	97
Alkali neutralised (equiv./mol.)	1·32	1·52	1·66	1·74	1·78

Methyl 2-*O*-methanesulphonyl-(α*β*)-D-arabinopyranoside :

Time (min.)	2	19	100	255	720
Alkali neutralised (equiv./mol.)	0·02	0·21	0·52	0·70	0·91

3-*O*-Methanesulphonyl-D-glucose :

Time (min.)	3	11	20	38	96
Alkali neutralised (equiv./mol.)	0·38	0·88	1·26	1·50	1·70

3-*O*-Methanesulphonyl-D-xylose :

Time (min.)	2·5	10·5	17·5	29	45
Alkali neutralised (equiv./mol.)	0·97	1·48	1·58	1·67	1·71

Methyl-3-*O*-methanesulphonyl-(α*β*)-D-glucopyranoside :

Time (min.)	5	27	95	237	450
Alkali neutralised (equiv./mol.)	0·05	0·23	0·58	0·77	0·85

Each benzylidene compound (0·03 millimol.) was dissolved in dioxan (10 c.c.) and 0·02N-sodium hydroxide (10 c.c.), and made up to 25 c.c. with water at room temperature; aliquot parts were titrated as above.

3 : 5-*O*-Benzylidene-4-*O*-formyl-2-*O*-methanesulphonyl-*aldehydo*-D-arabinose hydrate :

Time (min.)	2·5	5·5	16	58	107
Alkali neutralised (equiv./mol.)	2·73	3·04	3·44	3·79	3·97

4 : 6-*O*-Benzylidene-3-*O*-methanesulphonyl-D-glucose :

Time (min.)	1·7	8	20	50	115
Alkali neutralised (equiv./mol.)	1·66	2·65	3·05	3·24	3·49

Rate of Reaction of 2-O-*Methanesulphonyl-*D-*arabinose with Methanolic Sodium Methoxide.*—2-*O*-Methanesulphonyl-D-arabinose (0·20 millimol.) was dissolved in 0·01N-sodium methoxide in methanol (50 c.c.) at room temperature. Aliquot parts were withdrawn at the stated times, treated with a measured excess of standard acid, and back-titrated with 0·01N-sodium hydroxide to the end-point of phenol-red.

Time (min.)	60	120	164	420
Alkali neutralised (equiv./mol.)	0·32	0·48	0·59	0·72

Reaction of 4 : 6-O-*Benzylidene*-3-O-*methanesulphonyl*-D-*glucose with Sodium Hydroxide.*—This substance (0·00867 g.) was dissolved in dioxan (1 c.c.) and water (2 c.c.) and treated with 1 c.c. of 0·1N-sodium hydroxide (4 equiv./mol.). After 1 hr. samples removed for paper chromatography showed no Dische reaction, and the only detectable constituents were sodium formate (R_F 0·04) and a spot (R_F 0·82) giving a yellow colour with 2 : 4-dinitrophenylhydrazine hydrochloride. Extraction by ether yielded impure benzoic acid, m. p. 115—120°.

Reaction of 3 : 5-O-*Benzylidene*-4-O-*formyl*-2-O-*methanesulphonyl*-aldehydo-D-*arabinose Hydrate with Sodium Hydroxide.*—This substance (0·48 g.) was dissolved in methanol (30 c.c.) and diluted with water (150 c.c.), and N-sodium hydroxide (8 c.c.) was run in with stirring during 10 min. Liberated benzaldehyde was immediately extracted with ether and yielded the 2 : 4-dinitrophenylhydrazone (0·27 g.), m. p. 237—238°. The aqueous layer was acidified by passing it through a column of Amberlite IR-120 (H^+) (100 g.), then extracted continuously by ether. Evaporation of the extract yielded a syrupy mixture (0·04 g.). Paper chromatography showed the presence of at least four substances (R_F 0·33, 0·40, 0·50, and 0·80), all giving a pink colour with the hydroxylamine–ferric chloride spray reagent,[18] and hence probably all lactones of saccharinic acids.

THE UNIVERSITY, MANCHESTER. [*Received, February 11th,* 1957.]

[18] Smith and Abdel-Akher, *J. Amer. Chem. Soc.*, 1951, **73**, 5859.

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521. *An Approach to the Partial Synthesis of Aldosterone from Steroids lacking Substitution at* C_{18}.

By D. H. R. Barton, A. da S. Campos-Neves, and A. I. Scott.

3β-Acetoxyandrostane-11 : 17-dione, conveniently available by degradation of hecogenin, has been converted, by fission and subsequent reclosure of the 13—17 bond, and by other appropriate manipulations, into 18-benzylidene-3β-hydroxy-14-*iso* : 17-*iso-allo*pregnane-11 : 20-dione. Reduction of the 11-carbonyl group of the latter to 11β-hydroxyl, followed by ozonolytic cleavage of the benzylidene group, affords the masked aldehyde system characteristic of aldosterone.

Simpson, Tait, Wettstein, Neher, von Euw, Schindler, and Reichstein [1] have shown that aldosterone has the constitution and stereochemistry depicted in (I). In view of the minute amounts of the hormone available from natural sources its partial or total synthesis is of some importance. Indeed a total synthesis has recently been reported,[2] based upon the fundamental work of Sarett and his collaborators.[3] The power of modern methods of total steroid synthesis [3, 4] is such that the total synthesis of aldosterone may be easier than a partial synthesis from a steroid *lacking* an oxygenated or other functional group at position 18. There is, of course, also the possibility of partial synthesis from one of the few steroids, for example, conessine,[5] bearing a substituent at position 18.[6]

Some preliminary experiments on the opening of ring D of the steroid nucleus to permit modification of the 18-methyl group have appeared,[7, 8] but there is no published work on the introduction of the masked aldehyde (acetal) system of aldosterone (I) or on the reclosure of ring D. We have found a solution to the first of these problems and a possible, but laborious, solution to the second. Our starting point for the partial synthesis of aldosterone was to be an intermediate (or suitable derivative) available from the commercial process for the conversion of hecogenin into cortisone.[9]

The first series of experiments was based on 3β-acetoxyandrostane-11 : 17-dione [10] (II; R = Ac). Treatment with peracetic acid gave the lactone (III; R = Ac) which with dilute ethanolic potassium hydroxide furnished the unsaturated ketone (IV; R = H). The preferential fission of the ketone (II; R = Ac) at the 13—17 bond is in accord with prior knowledge.[7, 11] Reaction of the ketone (IV; R = H) with benzaldehyde in ethanolic hydrogen chloride followed by mild basic hydrolysis of the ethyl ester thus formed gave the benzylidene-acid (V; $n = 2$; R = H). This was homologated by the Arndt–Eistert procedure [12] to the acid (V; $n = 3$; R = H). The latter, on treatment with oxalyl chloride,[13] diazomethane, and then hydriodic acid [14] afforded the oily methyl ketone

[1] Simpson, Tait, Wettstein, Neher, von Euw, Schindler, and Reichstein, *Helv. Chim. Acta*, 1954, **37**, 1163, 1200.
[2] Schmidlin, Anner, Billeter, and Wettstein, *Experientia*, 1955, **11**, 365; Vischer, Schmidlin, and Wettstein, *ibid.*, 1956, **12**, 50.
[3] Sarett *et al.*, *J. Amer. Chem. Soc.*, 1952, **74**, 4974; 1953, **75**, 422; and later papers.
[4] Cardwell, Cornforth, Duff, Holtermann, and Robinson, *J.*, 1953, 361; Woodward, Sondheimer, Taub, Heusler, and McLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223; Stork, Loewenthal, and Mukharji, *ibid.*, 1956, **78**, 501; W. S. Johnson *et al.*, *ibid.*, p. 6278 and following papers; Wilds, Ralls, Tyner, Daniels, Kraychy, and Harnik, *ibid.*, 1953, **75**, 4878.
[5] Favre, Haworth, McKenna, Powell, and Whitfield, *J.*, 1953, 1115; and earlier papers.
[6] Cf. also Lábler, Černy, and Sorm, *Chem. and Ind.*, 1955, 1119; Uffer, *Helv. Chim. Acta*, 1956, **39**, 1834.
[7] Wendler, Taub, and Slates, *J. Amer. Chem. Soc.*, 1955, **77**, 3559.
[8] Heusser, Wohlfahrt, Müller, and Anliker, *Helv. Chim. Acta*, 1955, **38**, 1399; Anliker, Müller, Wohlfahrt, and Heusser, *ibid.*, p. 1404.
[9] Evans, Hamlet, Hunt, Jones, Long, Oughton, Stephenson, Walker, and Wilson, *J.*, 1956, 4356; Chapman, Elks, Phillips, and Wyman, *ibid.*, p. 4344; and earlier papers there cited.
[10] von Euw and Reichstein, *Helv. Chim. Acta*, 1942, **25**, 988.
[11] Murray, Johnson, Petersen, and Ott, *J. Amer. Chem. Soc.*, 1956, **78**, 981.
[12] Cf. Newman and Beal, *ibid.*, 1950, **72**, 5163.
[13] Shunk and Wilds, *ibid.*, 1948, **70**, 2427.
[14] Wolfrom and Brown, *ibid.*, 1943, **65**, 1516.

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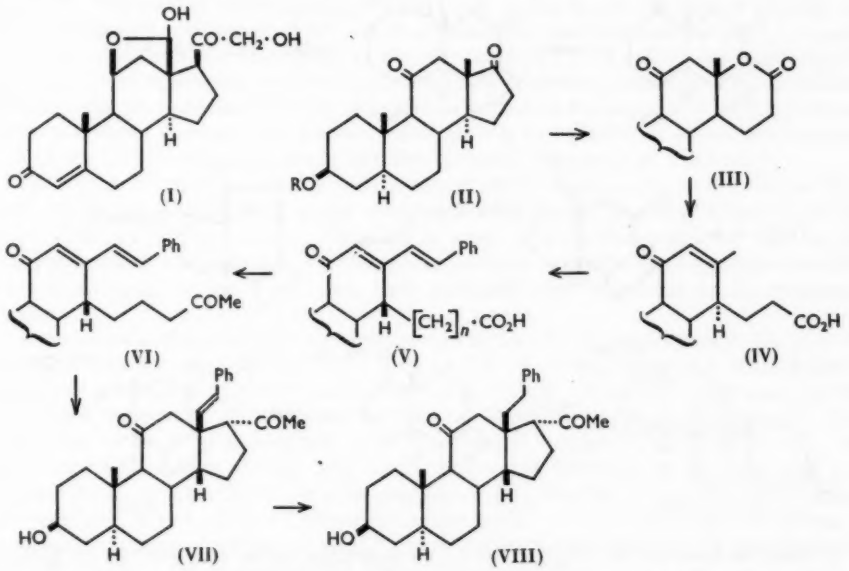
(VI; R = H). Without purification this compound was cyclised with mild base at room temperature to give 18-benzylidene-3β-hydroxy-14-*iso* : 17-*iso-allo*pregnane-11 : 20-dione (VII). This showed infrared bands at 3350 (OH), 1700 (11- and 20-ketones) and at 1630, 1600, 1585, 1494, 994, 747, and 694 cm.$^{-1}$ (*trans*-benzylidene).[15] It was further characterised by hydrogenation to the dihydro-derivative (VIII). Proof of the constitution and stereochemistry of (VII) is given later.



Since the yield in the homologation was unsatisfactory an alternative method for preparation of the acid (V; $n = 3$; R = H) was sought. The starting diketone (II; R = Ac) was converted into the cyanohydrin (or mixture of stereoisomeric cyanohydrins) and then, by hydrogenation and treatment with nitrous acid,[16] transformed into the D-homo-diketone (IX; R = Ac). Although this diketone did not react readily with peracetic acid, it was smoothly converted into the desired lactone (X; R = Ac) with trifluoroperacetic acid.[17] On treatment with benzaldehyde, etc., as before the lactone (X; R = Ac) gave the desired benzylidene-acid (V; $n = 3$; R = H) in a yield of 20—25% based on (IX; R = Ac). This procedure was, therefore, the method of choice for the preparation of the derivative (VII).

The constitution and stereochemistry of the benzylidene derivative (VII) were established as follows. Reduction with lithium aluminium hydride gave a triol (XI; R = H) which retained its benzylidene group as shown by the ultraviolet and infrared spectra [bands at 3350 (OH) and 1640, 1600, 1580, 1494, 998, 784, and 696 cm.$^{-1}$ (*trans*-benzylidene group)] and by ozonolysis under controlled conditions to give the masked aldehyde system (*no* carbonyl infrared absorption), typical (see above) of aldosterone, as in (XII; R = H). On Wolff-Kishner reduction this acetal afforded a new triol (XIII; R = H), characterised as its diacetate. The 11β-hydroxyl group was conveniently removed by catalytic hydrogenation in acetic acid over platinum in the presence of a trace of perchloric acid. The

[15] Cf. Sheppard and Simpson, *Quart. Rev.*, 1952, **6**, 1; A.P.I. Infra-red Spectrograms, No. 330.
[16] Goldberg *et al.*, *Helv. Chim. Acta*, 1940, **23**, 376, 840; 1941, **24**, 478, 295E; 1942, **25**, 1553, 1556; 1943, **26**, 1142.
[17] Sager and Duckworth, *J. Amer. Chem. Soc.*, 1955, **77**, 188; Emmons and Ferris, *ibid.*, 1953, **75**, 4623.

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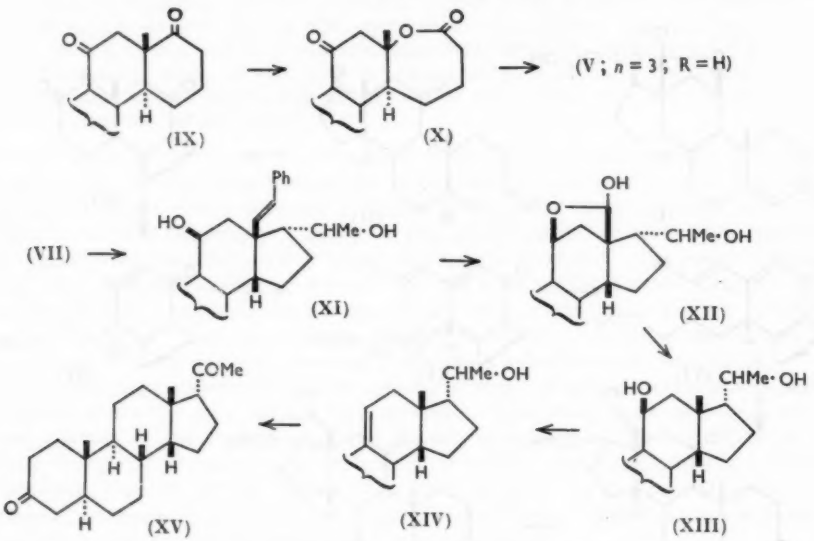
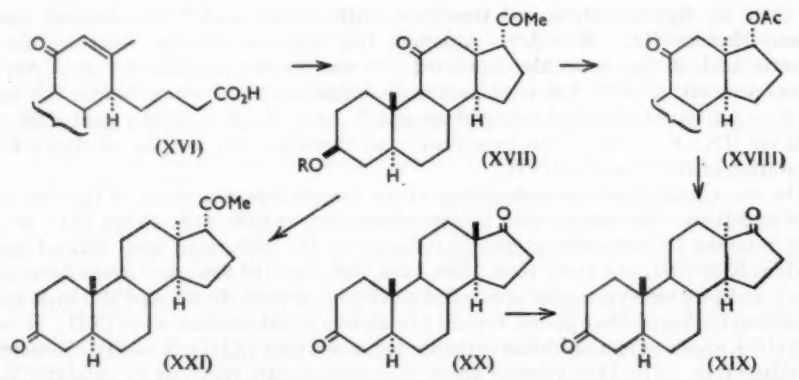
first step must be elimination of the 11β-hydroxyl group, to give (XIV; R = H), followed by further hydrogenation. The hydrogenation product (probably partially acetylated) was saponified and the resulting diol oxidised to the corresponding 3 : 20-dione. The latter was shown to be identical with an authentic specimen of 14-*iso* : 17-*iso*-*allo*pregnane-3 : 20-dione [18] (XV) kindly supplied by Professor T. Reichstein.



In order to examine the effect of the C_{14} configuration on the course of the cyclisation, the lactone (X; R = Ac) was treated under mild basic conditions to furnish the oily acid (XVI; R = H). The latter, when converted into the methyl ketone and cyclised with base as before, gave, after acetylation, a new diketone shown by the evidence that follows



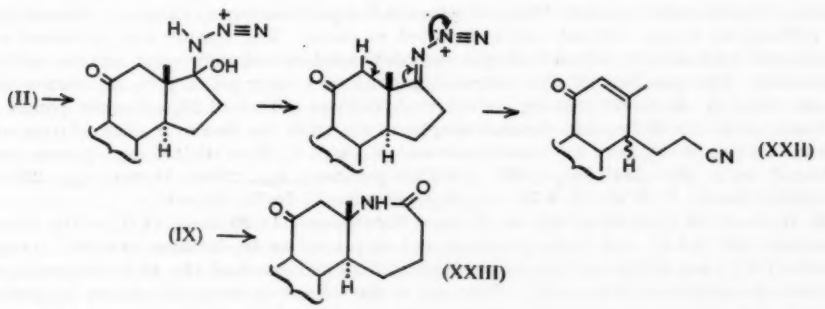
to be 3β-acetoxy-13-*iso* : 17-*iso*-*allo*pregnane-11 : 20-dione (XVII; R = Ac). The compound was further characterised by hydrolysis followed by oxidation to 13-*iso* : 17-*iso*-*allo*pregnane-3 : 11 : 20-trione. Treatment of the acetoxy-diketone (XVII; R = Ac)

[18] See Shoppee, *Helv. Chim. Acta*, 1944, **27**, 246; Press and Reichstein, *ibid.*, 1947, **30**, 2124.

with trifluoroperacetic acid gave the diacetate (XVIII; R = Ac). On reduction with lithium aluminium hydride, hydrogenation in the presence of perchloric acid, and further processing as in the case above, 13-*iso*androstane-3 : 17-dione [19] (XIX) resulted. Owing to incomplete removal of the 11β-oxygen function in this particular example some 13-*iso*-androstane-3 : 11 : 17-trione was also isolated. The authentic specimen of diketone (XIX) was obtained by irradiation of androstane-3 : 17-dione (XX) with ultraviolet light.[19,20] The configuration at C_{17} in (XVII; R = Ac) is not established directly by these experiments. However, if we accept a three-chair conformation for rings A, B, and C, then the more stable configuration of the side chain of (XVII; R = Ac), which would surely be the configuration produced from its mode of genesis, would be 17α; as already written. The acetoxy-dione (XVII) was also subjected to the procedure for the removal of the 11-oxygen function (see above). This gave a new diketone, 13-*iso*-*allo*pregnane-3 : 20-dione (XXI) showing a single infrared carbonyl frequency at 1700 cm.$^{-1}$.

The results obtained on the stereochemistry of the cyclisation process become rational if the cyclisation is controlled by the configuration at C_{14}. This would require that the 14-side-chain of (V; $n = 2$ or 3; R = H) is more stable in the quasiaxial than in the quasiequatorial configuration.[21,22] This is conceivable since the quasiequatorial 14-side-chain is hindered by the 7—8 bond, such hindrance not obtaining in its quasiaxial analogue.

Some investigation was made on the cleavage of the 13—17 bond through the Schmidt reaction.[23] 3β-Acetoxyandrostane-11 : 17-dione (II; R = Ac), under the usual Schmidt conditions, afforded mainly the unsaturated nitrile (XXII; R = Ac), presumably by the mechanism indicated. The Schmidt reaction on 3β-acetoxy-D-homoandrostane-11 : 17*a*-dione (IX; R = Ac), in contrast, gave the desired lactam (XXIII; R = Ac). On treatment with sodium acetate and acetic anhydride followed by benzaldehyde and ethanolic hydrogen chloride in the usual way (see above), this furnished the known benzylidene-acid (V; $n = 3$; R = H) although in poor yield. This confirms that the lactam is produced by rupture of the 13—17 bond.[8] Some further transformation products involving Schmidt reactions are recorded in the Experimental section.



Experimental

$[\alpha]_D$ are in $CHCl_3$ unless stated otherwise; ultraviolet absorption spectra refer to EtOH solutions. Infrared spectra were kindly determined by Dr. G. Eglinton and his colleagues, for Nujol suspensions unless specified to the contrary. The alumina for chromatography was

[19] Billeter and Miescher, *Helv. Chim. Acta.*, 1951, **34**, 2053.
[20] Butenandt *et al.*, *Ber.*, 1941, **74**, 1308; 1942, **75**, 1931; 1944, **77**, 392, 394.
[21] Cf. Barton, *J.*, 1953, 1027.
[22] Cf. Barton, Cookson, Klyne, and Shoppee, *Chem. and Ind.*, 1954, 21.
[23] Wolff, "Organic Reactions," Vol. III, p. 307; Smith, *J. Amer. Chem. Soc.*, 1954, **76**, 431; and many earlier papers.

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Brockmann Grade III. Light petroleum refers to the fraction of b. p. 40—60° unless stated otherwise.

3β-*Acetoxy*-13-*hydroxy*-11-*oxo*-13(17)-seco*androstan*-17-*oic Lactone* (III; R = Ac).—3β-Acetoxyandrostane-11 : 17-dione, m. p. 162—163°, $[\alpha]_D$ +95° (*c* 1·16 in dioxan) (2·0 g.), in " AnalaR " acetic acid (10 ml.) was treated with peracetic acid (4·0 g.) in the same solvent (20 ml.) containing toluene-*p*-sulphonic acid (20 mg.) at 7—10° for 120 hr. (negative test with ethanolic 2 : 4-dinitrophenylhydrazine reagent). Cautious addition of water gave the *lactone* (III; R = Ac) (1·10 g.), m. p. (needles from aqueous methanol) 218—219°, $[\alpha]_D$ −22° (*c* 1·81) (Found: C, 69·6; H, 8·3. $C_{21}H_{30}O_5$ requires C, 69·6; H, 8·35%). Further dilution gave additional lactone (420 mg.).

3β-*Hydroxy*-11-*oxo*-13(17)-seco*androst*-12-*ene*-17-*carboxylic Acid* (IV; R = H).—The above-mentioned lactone (1·07 g.) in ethanol (49 ml.) was treated with potassium hydroxide (800 mg.) in ethanol (200 ml.), and the appearance of a max. at 239 mμ followed spectrophotometrically (ε constant at 10,300 after 45 min.). The acidic *product* (1·0 g.) gave, on crystallisation from ether, needles, m. p. 155°, $[\alpha]_D$ −4° (*c* 2·01; 1·76), $\lambda_{max.}$ 239 mμ (ε 13,600) (Found: C, 71·05; H, 8·75. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%).

This acid (260 mg.) in ethanolic hydrogen chloride (25 ml.; 40% w/w) containing benzaldehyde (250 mg.; redistilled) was left at 20°, the appearance of a max. at 320 mμ being followed spectrophotometrically (ε constant at 29,000 after 16 hr.). Addition of water (cooling), extraction into ether, and washing with saturated sodium hydrogen sulphite solution gave the oily ethyl ester. Treated with potassium hydroxide (1·0 g.) in ethanol (50 ml.) containing water (1·0 ml.) at room temperature for 16 hr., this furnished 18-*benzylidene*-3β-*hydroxy*-11-*oxo*-13(17)-seco*androst*-12-*ene*-17-*carboxylic acid* (V; *n* = 2; R = H) (130 mg.), m. p. (from methanol) 237—238°, $[\alpha]_D$ +320° (*c* 1·25 in pyridine), $\lambda_{max.}$ 240 (ε 10,600), 325 mμ (ε 34,200) (Found: C, 76·4; H, 8·3. $C_{26}H_{32}O_4$ requires C, 76·45; H, 7·9%). The neutral fraction (40 mg.), on rehydrolysis, gave further acid (25 mg.).

18-*Benzylidene*-3β-*hydroxy*-11-*oxo*-13(17)-seco*androst*-12-*en*-17-*ylacetic Acid* (V; *n* = 3; R = H).—The acid described in the preceding paragraph (1·64 g.) in dry benzene (7·0 ml.) was treated with oxalyl chloride (3·0 g.) in benzene (3·0 ml.) at room temperature for 16 hr. Removal of the solvent *in vacuo* gave an oil. This in benzene (7·0 ml.) was added dropwise to diazomethane (2·0 g.) in ether (200 ml.) at 5°. After 45 min. the solvent was removed *in vacuo* at <40° to give the desired diazo-ketone (1·5 g.). Without further purification this ketone, in methanol (50 ml.), was kept at 46—48° during the addition with stirring of silver benzoate–triethylamine catalyst [12] (2·5 ml. added in five portions during 15 min.). The mixture was refluxed for 5 min., filtered, and evaporated *in vacuo*. The residue was extracted into benzene and washed with sodium hydrogen carbonate solution and with water, and the solution evaporated. The resultant oil was chromatographed over silica gel to give, on elution with benzene–ether (1 : 1), an oil (200 mg.) which on hydrolysis (50 ml. of 2% ethanolic potassium hydroxide at 20° for 16 hr.) and chromatography of the acidic fraction over silica [elution with benzene–acetone (9 : 1)] gave the homologous *acid* (V; *n* = 3; R = H) (175 mg.), prisms (from methanol), m. p. 233—234°, $[\alpha]_D$ +301° (*c* 0·82 in pyridine), $\lambda_{max.}$ 238 (ε 14,000), $\lambda_{max.}$ 325 mμ (ε 35,200) (Found: C, 77·0; H, 7·75. $C_{27}H_{34}O_4$ requires C, 76·75; H, 8·1%).

3β-*Hydroxy*-18-*benzylidene*-14-iso: 17-iso-allo*pregnane*-11 : 20-*dione* (VII).—The above-mentioned acid (1·0 g.) was finely powdered and suspended in dry benzene (5·0 ml.) Oxalyl chloride (1·0 g.) was added and the mixture left until all had dissolved (3—40 hr. depending on the state of subdivision of the acid). Removal of the solvent *in vacuo*, dissolution in benzene (5·0 ml.), and addition to diazomethane (2·0 g.) in ether (150 ml.) at 0—5°, storage for 2 hr., and then removal of the excess of ethereal diazomethane at <40°, gave an oily diazo-ketone. This was taken up in chloroform and shaken with 55% aqueous hydriodic acid solution (1·0 ml.) for 5 min., to furnish an oily methyl ketone. The latter (1·0 g.) in benzene (3·0 ml.) was treated with 0·2N-ethanolic potassium hydroxide (100 ml.) at room temperature for 16 hr. under nitrogen {$[\alpha]_D$ constant at +57° (*c* 1·0), replacement of max. at 235 and 325 mμ by a band at 255 mμ (ε 12,000)} to give 18-*benzylidene*-3β-*hydroxy*-14-iso: 17-iso-allo*pregnane*-11 : 20-*dione* (VII). Purified by chromatography over silica gel in benzene–ether (9 : 1) and sublimation at 160°/10^{-5} mm. this (250 mg.) formed needles (from ether), m. p. 194—195°, $[\alpha]_D$ −26° (*c* 0·84), $\lambda_{max.}$ 255 mμ (ε 20,900), inflex. at 284 and 293 mμ (ε 2600 and 1800 respectively) (Found: C, 80·05; H, 8·4. $C_{28}H_{36}O_3$ requires C, 79·95; H, 8·65%). On hydrogenation (62 mg.) over 10% palladized charcoal (20 mg.) in ethyl acetate (5·0 ml.) for 24 hr. (0·96 mol. absorbed), this

furnished 18-*benzyl*-3β-*hydroxy*-14-iso : 17-iso-allo*pregnane*-11 : 20-*dione* (VIII), plates (from ether), m. p. 193—194°, $[\alpha]_D$ 0° (*c* 1·00), no styryl absorption in the ultraviolet region (Found : C, 79·6; H, 8·9. $C_{28}H_{38}O_3$ requires C, 79·6; H, 9·05%).

3β-*Acetoxy*-D-*homoandrostane*-11 : 17a-*dione* (IX; R = Ac).—3β-Acetoxyandrostane-11 : 17-dione (5·5 g.) in absolute ethanol (138 ml.) was treated with " AnalaR " potassium cyanide (33 g.) and kept at 0—5° with efficient stirring and addition during 1 hr. of " AnalaR " acetic acid (35·75 ml.). The resultant paste was stirred for a further 1½ hr. and poured into water (1 l.). The precipitate of mixed cyanohydrins, m. p. 103—106°, $[\alpha]_D$ −6° (*c* 2·3), was filtered after 30 min. and dried (5·8 g.) over phosphoric oxide *in vacuo* for 24 hr. at not more than room temperature. This material (5·8 g.) in " AnalaR " acetic acid (160 ml.) was hydrogenated over platinum (2·0 g.) (2 mols. uptake in 40 min.). The catalyst was removed by filtration, and the solution concentrated *in vacuo* on the steam-bath to 25 ml. and then diluted with water to 250 ml. Care must be taken during the concentration of the acetic acid solution that the temperature does not rise too high and that the heating is not too prolonged. In one experiment (with Dr. M. Martin-Smith) the primary amino-group was acetylated during the evaporation, to afford 17ξ-*acetamidomethyl*-3β-*acetoxy*-17ξ-*hydroxyandrostan*-11-*one*, plates (from methanol), m. p. 258—260°, $[\alpha]_D$ +10° (*c* 2·28), infrared max. at 3305 (NH), 3270 (OH), 1720 and 1242 (acetate), 1700 (11-ketone), and 1640 and 1547 cm.$^{-1}$ (CO·NH) (Found : C, 68·7; H, 8·9; N, 3·35; Ac, 20·5. $C_{24}H_{37}O_5N$ requires C, 69·45; H, 8·8; N, 3·55; Ac, 20·3%). The amine solution (see above) was treated at 0—5° with 10% sodium nitrite solution (36 ml.) at the same temperature for 3 hr. Extraction with chloroform and chromatography over alumina (100 g.) gave, on elution with benzene, 3β-*acetoxy*-D-*homoandrostane*-11 : 17a-*dione* (IX; R = Ac) (4·24 g.), prisms [from ethyl acetate–light petroleum (b. p. 60—80°)], m. p. 185—186°, $[\alpha]_D$ −29° (*c* 1·79) (Found : C, 73·55; H, 8·75. $C_{22}H_{32}O_4$ requires C, 73·3; H, 8·95%).

3β-*Acetoxy*-13-*hydroxy*-11-*oxo*-13(17a)-seco-D-*homoandrostan*-17-*oic Lactone* (X; R = Ac).—3β-Acetoxy-D-homoandrostane-11 : 17*a*-dione (1·05 g.) in methylene dichloride (10 ml.) containing toluene-*p*-sulphonic acid (10 mg.) was treated with stirring with trifluoroperacetic acid (715 mg., 2 equiv.) in the same solvent (5 ml.) during 10 min. at <5°. The stoppered reaction flask was stored at 20° in the dark for 70 min. (1 equiv. consumed). The solution was diluted with chloroform (25 ml.) and washed very rapidly with water (50 ml.), saturated sodium hydrogen carbonate (50 ml.) and water (50 ml.). Trituration of the oily product with ether afforded the *lactone* (X; R = Ac) (500 mg.), needles (from ether), m. p. 182—183°, $[\alpha]_D$ −66° (*c* 1·05) (Found : C, 70·8; H, 8·5. $C_{22}H_{32}O_5$ requires C, 70·2; H, 8·6%). For routine preparations the total crude lactone (see above) was suitable for the conversion described in the sequel.

This lactone was treated with benzaldehyde as in the procedure described above. The acidic product, chromatographed over silica [elution with benzene–acetone (9 : 1)] gave 18-benzylidene-3β-hydroxy-11-oxo-13(17)-*seco*androst-12-ene-17-ylacetic acid (see above), identified by m. p., mixed m. p., rotation, and infrared spectrum. The overall yield from 3β-acetoxy-D-homoandrostane-11 : 17*a*-dione was 20—25%.

18-*Benzylidene*-14-iso : 17-iso-allo*pregnane*-3β : 11β : 20ξ-*triol* (XI; R = H).—18-Benzylidene-3β-hydroxy-14-*iso* : 17-*iso-allo*pregnane-11 : 20-dione (see above) (400 mg.) was extracted with dry ether from a Soxhlet thimble into lithium aluminium hydride (400 mg.) in the same solvent (150 ml.). Decomposition of the excess of reductant with ethyl acetate and isolation in the usual way afforded 18-*benzylidene*-14-iso : 17-iso-allo*pregnane*-3β : 11β : 20ξ-*triol* (XI; R = H) (300 mg.), prisms (from ethyl acetate), m. p. 237—238°, $[\alpha]_D$ +59° (*c* 1·50), +58° (*c* 1·00), $\lambda_{max.}$ 255 mμ (ε 20,800) (Found : C, 79·05; H, 9·05. $C_{28}H_{40}O_3$ requires C, 79·2; H, 9·5%).

3β : 11β : 20ξ-*Trihydroxy*-14-iso : 17-iso-allo*pregnan*-18-*al* (cf. XII; R = H).—The benzylidene-triol described above (101 mg.) in methylene dichloride (100 ml.) was ozonised at −60° until the styrene absorption band at 255 mμ had been replaced by a band of lower intensity at 245 mμ (ε 11,000) (spectrophotometric control by removal of aliquot parts). The solution was stirred with zinc dust (500 mg.; freshly activated with acetic acid) and 80% acetic acid (5 ml.) whilst the temperature rose from −60° to +20° (2 hr.). Crystallisation of the product from chloroform furnished the *product* (cf. XII; R = H), needles, m. p. 208—210°, $[\alpha]_D$ +106° (*c* 1·30 in MeOH), no ultraviolet absorption, no infrared carbonyl absorption (Found : C, 72·2; H, 9·65. $C_{21}H_{34}O_4$ requires C, 71·95; H, 9·8%).

This masked aldehyde (150 mg.) was added to a mixture of sodium ethoxide (300 mg.) in absolute ethanol (3 ml.) and anhydrous hydrazine (1·5 ml.) and heated at 180° for 16 hr.

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Isolation of the product in the usual way afforded 14-iso : 17-iso-allo*pregnane*-3β : 11β : 20ξ-*triol* (XII; R = H) (140 mg.), prisms (from ethyl acetate), m. p. 202—203°, $[\alpha]_D$ +59° (*c* 0·73) (Found: C, 75·15; H, 10·8. $C_{21}H_{36}O_3$ requires C, 74·95; H, 10·8%). Treatment with pyridine–acetic anhydride overnight at room temperature gave the 3β : 20ξ-*diacetate*, needles (from methanol), m. p. 181—184°, $[\alpha]_D$ +45° (*c* 0·70) (Found: C, 71·75; H, 9·35. $C_{25}H_{40}O_5$ requires C, 71·4; H, 9·6%).

14-*iso* : 17-*iso-allo*Pregnane-3β : 11β : 20ξ-triol (see above) (140 mg.) in " AnalaR " acetic acid (20 ml.) containing 71% aqueous perchloric acid (0·2 ml.) was hydrogenated over pre-reduced platinum catalyst (70 mg.) for 24 hr. (absorption of 1 mol. of hydrogen). The product was hydrolysed by refluxing 5% methanolic potassium hydroxide (25 ml.), to give 14-*iso* : 17-*iso-allo*pregnane-3β : 20ξ-diol (125 mg.), needles (from methanol), m. p. 163—164°, $[\alpha]_D$ +43° (*c* 2·30). The diol (125 mg.) in " AnalaR " acetic acid (2 ml.) was treated with chromium trioxide (99·0 mg.) in the same solvent (6 ml.) for 16 hr. at room temperature. The product was chromatographed over alumina (grade 3; 3 g.). Elution with light petroleum (b. p. 60—80°)–benzene (9 : 1) gave 14-*iso* : 17-*iso-allo*pregnane-3 : 20-dione (XV) (48 mg.), needles (from light petroleum), m. p. 139—141°, $[\alpha]_D$ +39° (*c* 1·10), identified by m. p., mixed m. p., rotation, and infrared spectrum (KCl disc). The authentic specimen had m. p. 137—139°, $[\alpha]_D$ +40°.

Action of Base on 3β-*Acetoxy*-13-*hydroxy*-11-*oxo*-13(17a)-seco-D-*androstan*-17-*oic Lactone*.—The lactone (1·95 g.) in 5% ethanolic potassium hydroxide solution (100 ml.) was refluxed under nitrogen for 1 hr. Separation into acid and neutral fractions gave in the former an acidic oil (1·80 g.), showing $\lambda_{max.}$ 237 mμ (ε 12,600). This acid was transformed, without isolation of intermediates, into the corresponding methyl ketone and then cyclised (spectrophotometric control) by the processes already described. The cyclised diketone was acetylated (1·10 g.) and then chromatographed over alumina. Elution with benzene afforded 3β-*acetoxy*-13-iso : 17-iso-allo*pregnane*-11 : 20-*dione* (XVII; R = Ac) (200 mg.), needles [from light petroleum (b. p. 60—80°)], m. p. 121—122°, $[\alpha]_D$ −182° (*c* 1·10) (Found: C, 73·8; H, 8·8. $C_{23}H_{34}O_4$ requires C, 73·75; H, 9·15%). This acetoxy-dione (300 mg.) was hydrolysed with 5% methanolic potassium hydroxide for 3 hr. on the steam-bath, and the resultant 3β-hydroxy-compound (200 mg.) in " AnalaR " acetic acid (10 ml.) oxidised by chromium trioxide (200 mg.) overnight at room temperature, to give 13-iso : 17-iso-allo*pregnane*-3 : 11 : 20-*trione* (150 mg.), needles (from ethyl acetate–light petroleum), m. p. 140°, $[\alpha]_D$ −165° (*c* 0·85) (Found: C, 76·5; H, 9·25. $C_{21}H_{30}O_3$ requires C, 76·3; H, 9·15%).

3β-Acetoxy-13-*iso* : 17-*iso-allo*pregnane-11 : 20-dione (300 mg.) in dry ether (20 ml.) was reduced with lithium aluminium hydride (300 mg.) in the same solvent (180 ml.) under reflux overnight. The product (260 mg.) in " AnalaR " acetic acid (20 ml.) containing 72% perchloric acid (0·2 ml.) was hydrogenated over pre-reduced platinum catalyst (130 mg.) for 24 hr. (1 mol. uptake). The product was hydrolysed with methanolic potassium hydroxide, and the resultant diol (230 mg.) oxidised with chromium trioxide (200 mg.) in " AnalaR " acetic acid (15 ml.) for 16 hr. at room temperature. The oily dione (100 mg.) was chromatographed over alumina in carbon tetrachloride, to give 13-iso : 17-iso-allo*pregnane*-3 : 20-*dione*, needles (from light petroleum), m. p. 147—148°, $[\alpha]_D$ −61° (*c* 0·75) (Found: C, 79·6; H, 10·2. $C_{21}H_{32}O_2$ requires C, 79·7; H, 10·2%).

3β-Acetoxy-13-*iso* : 17-*iso-allo*pregnane-11 : 20-dione (240 mg.) in methylene dichloride (4 ml.) was treated with trifluoroperacetic acid (150 mg.) in the same solvent (1·0 ml.) for 1·5 hr. at room temperature to furnish 3β : 17α-*diacetoxy*-13-iso*androstan*-11-*one* (XVIII; R = Ac) (200 mg.). On purification by chromatography over alumina elution with benzene–light petroleum mixtures, this (130 mg.) formed needles (from light petroleum), m. p. 123°, $[\alpha]_D$ −125° (*c* 1·10) (Found: C, 70·5; H, 8·95. $C_{23}H_{34}O_5$ requires C, 70·75; H, 8·8%). This diacetate (300 mg.) was reduced with lithium aluminium hydride, hydrogenated, and oxidised as described above. The product was chromatographed over alumina in carbon tetrachloride. Elution with that solvent gave 13-*iso*androstane-3 : 17-dione (XIX) (30 mg.), needles (from light petroleum), m. p. 165—167°, $[\alpha]_D$ −74° (*c* 0·38), identical (m. p., mixed m. p., rotation, and infrared spectrum) with an authentic specimen (see below). Development of the chromatogram with benzene–light petroleum (1 : 1) gave 13-iso*androstane*-3 : 11 : 17-*trione* (77 mg.), needles or prisms (from ether–light petroleum), m. p. 174—175°, $[\alpha]_D$ −160° (*c* 2·00) (Found: C, 75·4; H, 8·7. $C_{19}H_{26}O_3$ requires C, 75·45; H, 8·65%).

The authentic specimen of 13-*iso*androstane-3 : 17-dione was obtained by the following

procedure.[19, 20] Androstane-3 : 17-dione (XX) (495 mg.) in benzene (30 ml.) was irradiated in a silica tube with ultraviolet light for 23 hr. (rotational change from +104° to +16°). Chromatography over alumina and elution with carbon tetrachloride gave authentic 13-*iso*androstane-3 : 17-dione, m. p. 167—168°, $[\alpha]_D$ −76° (*c* 0·63) (Found : C, 79·3; H, 9·4. Calc. for $C_{19}H_{28}O_2$: C, 79·1; H, 9·8%). Billeter and Miescher [19] reported m. p. 165—166°, $[\alpha]_D$ −58° (*c* 0·60).

Bromination of 3β-*Acetoxy*-D-*homoandrostane*-11 : 17a-*dione*.—The diketone (1·0 g.) in " AnalaR " acetic acid (22 ml.) containing hydrogen bromide (50% in acetic acid; 5 drops) was treated with bromine (446 mg.) in the same solvent (18·7 ml.) for 1 min. (discharge of colour). Crystallisation of the product from ethyl acetate–light petroleum furnished 3β-*acetoxy*-17α-*bromo*-D-*homoandrostane*-11 : 17a-*dione* (975 mg.), needles, m. p. 225—227° (decomp.), $[\alpha]_D$ +24° (*c* 2·00), infrared max. at 1735 (acetate), 1725 (equatorial α-bromo-ketone), and 1710 cm.$^{-1}$ (11-ketone) (Found : C, 60·4; H, 7·3; Br, 18·2. $C_{23}H_{31}O_4Br$ requires C, 60·15; H, 7·1; Br, 18·15%). This bromo-ketone was recovered unchanged after treatment with trifluoroperacetic acid.

The bromo-ketone (800 mg.) was refluxed with collidine (20 ml.) for 15 min. Filtration of the product in benzene solution through alumina gave 3β-*acetoxy*-D-*homoandrost*-16-*ene*-11 : 17a-*dione* (300 mg.), needles (from ether), m. p. 170—172°, $[\alpha]_D$ −32° (*c* 2·30), $\lambda_{max.}$ 225 mμ (ε 8200) (Found : C, 73·9; H, 8·15. $C_{23}H_{30}O_4$ requires C, 73·7; H, 8·45%). Treatment with pyridine–hydroxylamine hydrochloride overnight at room temperature furnished the 17a-*monoxime*, m. p. (from aqueous methanol) 237—239°, $[\alpha]_D$ −166° (*c* 1·12 in pyridine), $\lambda_{max.}$ 236 mμ (ε 8400) (Found : C, 70·9; H, 8·3; N, 3·95. $C_{23}H_{31}O_4N$ requires C, 70·75; H, 8·35; N, 3·75%).

Bromination of 3β-*Acetoxyandrostane*-11 : 17-*dione*.—The diketone (1·0 g.) in " AnalaR " acetic acid (20 ml.) containing hydrogen bromide (50% in acetic acid; 5 drops) was treated with bromine (463 mg.) in the same solvent (13·1 ml.) for 1 hr. The product, after crystallisation from ethyl acetate, was a mixture of mono- and di-bromide. Further fractionation gave 3β-*acetoxy*-16ξ-*bromoandrostane*-11 : 17-*dione*, plates (from ethyl acetate), m. p. 183—185°, $[\alpha]_D$ +125° (*c* 1·06), infrared max. at 1730 (acetate and *cyclo*pentanone) and 1705 cm.$^{-1}$ (11-ketone) (Found : C, 58·9; H, 6·65. $C_{21}H_{29}O_4Br$ requires C, 59·3; H, 6·85%). This bromo-ketone was recovered unchanged after treatment with trifluoroperacetic acid.

Schmidt Reaction on 3β-*Acetoxyandrostane*-11 : 17-*dione*.—The diketone (344 mg.) in chloroform (7·0 ml.) and " AnalaR " concentrated sulphuric acid (2·0 ml.) was treated, at 0° with stirring, with sodium azide (97 mg.) portionwise. The stirring was continued for 30 min. Chromatography of the product over alumina (6 g.) and elution with benzene gave 3β-*acetoxy*-11-*oxo*-13(17)-seco*androst*-12-*ene*-17-*nitrile* (XXII; R = Ac), needles, m. p. 138° or 155—157°, $[\alpha]_D$ −55° (*c* 1·07), $\lambda_{max.}$ 234, 311—315 (ε 7200 and 27 respectively) (Found : C, 73·25; H, 8·1; N, 3·85. $C_{21}H_{29}O_3N$ requires C, 73·45; H, 8·5; N, 4·1%). Elution with benzene–methanol (4 : 1) gave a small quantity (20 mg.) of a lactam, m. p. 305—307° (sublimes), which was not investigated.

3β-*Acetoxy*-17b-*aza*-D-*bishomoandrostane*-11 : 17a-*dione*.—3β-Acetoxy-11 : 17*a*-dioxo-D-homoandrostane (720 mg.) in chloroform (14 ml.) and " AnalaR " concentrated sulphuric acid (4·0 ml.) was treated at 0—5° with sodium azide (200 mg.) in small portions. Working up after 30 min. gave 3β-*acetoxy*-17b-*aza*-D-*bishomoandrostane*-11 : 17a-*dione* (XXIII), plates (from methanol), m. p. 278—279°, $[\alpha]_D$ −77° (*c* 1·01), infrared max. at 1727 (acetate), 1706 (11-ketone), and 1667 cm.$^{-1}$ (lactam) (Found : C, 70·05; H, 8·5; N, 3·95. $C_{23}H_{33}O_4N$ requires C, 70·35; H, 8·85; N, 3·75%). The lactam (1·0 g.) was refluxed for 5 hr. with acetic anhydride (50 ml.) and fused sodium acetate (3·0 g.). Separation into acid and neutral fractions gave, in the former, an oil (396 mg.), $\lambda_{max.}$ 237 mμ (ε 5100), and, in the latter, a product (600 mg.), $\lambda_{max.}$ 237 mμ (ε 6400). The crude acid fraction was treated with benzaldehyde and further processed as above, to give 18-benzylidene-3β-hydroxy-11-oxo-13(17)-*seco*androst-12-en-17-ylacetic acid, identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +294° (*c* 0·37 in pyridine)}, and infrared spectrum.

3β-*Acetoxy*-17α-*bromo*-17b-*aza*-D-*bishomoandrostane*-11 : 17a-*dione*.—The appropriate 17α-bromo-dione (see above) (3·1 g.) in chloroform (60 ml.) and " AnalaR " concentrated sulphuric acid (16·8 ml.) was treated with sodium azide (730 mg.) as in the cognate preparation reported above. Crystallisation from ethyl acetate gave 3β-*acetoxy*-17α-*bromo*-17b-*aza*-D-*bishomoandrostane*-11 : 17a-*dione* (3·0 g.), prisms, m. p. 183—185°, $[\alpha]_D$ −12° (*c* 1·09) (Found : C, 58·15; H, 6·8; N, 3·45; Br, 17·9. $C_{22}H_{32}O_4NBr$ requires C, 58·1; H, 7·1; N, 3·1; Br, 17·6%). This

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bromo-lactam (560 mg.) was refluxed with collidine for 15 min., to furnish, on chromatography over alumina and elution with ether–methanol (9 : 1), 3β-*acetoxy*-17b-*aza*-D-*bishomoandrost*-16-*ene*-11 : 17a-*dione*, prisms (from ethyl acetate), m. p. 262°, $[\alpha]_D$ −95° (*c* 0·92); in the ultraviolet absorption spectrum a shoulder was found at 230—240 mμ (ε 3000),[24] infrared max. at 1725 (acetate), 1711 (11-ketone), and 1675 (lactam) cm.$^{-1}$ (Found: C, 70·7; H, 8·6; N, 4·1. $C_{22}H_{31}O_4N$ requires C, 70·75; H, 8·4; N, 3·75%).

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[24] Cf. Edwards and Singh, *Canad. J. Chem.*, 1954, **32**, 683.

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522. *Bisquaternary Ammonium Salts. Part III.* 4-Alkylbenzene-1 : ω-bistrialkylammonium Salts.*

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A series of 4-alkylbenzene-1 : ω-bistrialkylammonium di-iodides (I) (where R = R′ = R″ = Me or Et and *n* is 0—6) has been prepared. Some of these compounds are of interest as ganglion or neuromuscular blocking agents.

THE work described in this paper was undertaken in 1950—1952 in the hope of obtaining compounds of greater pharmacological value than the well-known polymethylene bisquaternary ammonium salts.[1,2] The first two compounds prepared (I; R = R′ = R″ = Me; *n* = 0 and 1) have no ganglion-blocking activity, but the next member of the series (*n* = 2) is very active. Ganglion-blocking activity was retained where *n* = 3, but higher homologues (*n* = 4—6) were found, as expected, to be predominantly neuromuscular

(I) p-$R''R'RN^+{\cdot}C_6H_4{\cdot}[CH_2]_n{\cdot}N^+RR'R''$ $2I^-$

blocking agents. Members of some related homologous series (I; R = R′ = Me, R″ = Et; R = Me; R′ = R″ = Et; R = R′ = R″ = Et) have also been prepared. Details of the pharmacological work have been published,[3] and some of the compounds are the subject of patent specifications.[4] The synthesis of 4-ethylbenzene-1 : 2′-bis(trimethylammonium iodide) (I; R = R′ = R″ = Me; *n* = 2) was described by Borovička *et al.*[5] after the completion of the present work.

Hoffmann [6] first described, though inadequately, the preparation of *p*-phenylenebis(trimethylammonium iodide) (I; R = R′ = R″ = Me; *n* = 0). In the present work, tetra-*N*-methyl-*p*-phenylenediamine,[7] prepared from *p*-phenylenediamine by the Eschweiler–Clarke reaction, readily furnished the monoquaternary salt [8] when treated with methyl iodide. It is not surprising (cf. Fahim and Galaby [9]) that this compound was converted into the bisquaternary derivative only under drastic conditions; when it was treated with methyl iodide in ethylene glycol at 100° (sealed tube) for less than 70 hr., unchanged

* Part II, *J.*, 1956, 3941.

[1] Barlow and Ing, *Brit. J. Pharmacol.*, 1948, **3**, 298.
[2] Paton and Zaimis, *ibid.*, 1949, **4**, 381.
[3] Wien and Mason, *ibid.*, 1953, **8**, 306.
[4] Leeds and Ashley, B.P. 705,506, 705,528, 748,217; Wien, Ashley, and Leeds, B.P. 748,214.
[5] Borovička, Šedivý, Jílek, and Protiva, *Chem. Listy*, 1955, **49**, 231.
[6] Hofmann, *Compt. rend.*, 1863, **56**, 992.
[7] Meyer, *Ber.*, 1903, **36**, 2979.
[8] Pinnow and Pistov, *Ber.*, 1894, **27**, 603.
[9] Fahim and Galaby, *J.*, 1950, 3529.

monoquaternary compound remained. 4-Methylbenzene-1 : 1′-bis(trimethylammonium iodide) (I; R = R′ = R″ = Me; $n = 1$) was obtained without difficulty on treating *p*-dimethylaminobenzylamine [10] with methyl iodide and sodium carbonate in boiling methanol.

No difficulty was experienced in the preparation of the important ganglionic blocking agent 4-ethylbenzene-1 : 2′-bis(trimethylammonium iodide) (I; R = R′ = R″ = Me; $n = 2$) from *p*-dimethylaminophenethylamine, methyl iodide, and sodium carbonate in boiling methanol. Braun and Blessing [11] claimed to have prepared this compound from both *p*-amino- and *p*-dimethylamino-phenethylamine. No details were given but it was stated that experiments with *p*-aminophenethylamine gave erratic results (cf. Borovička *et al.*[5]). However, we have had no difficulty in preparing the compound in one operation from either starting material. The product obtained by Braun and Blessing [11] from *p*-dimethylaminophenethylamine is described as having m. p. >300°. Our product had m. p. 255°, and this agrees with that recorded (259—260°) by Borovička *et al.*[5] who also comment on the high m. p. given by the German workers. In the present work *p*-aminophenethylamine was prepared by catalytic reduction of *p*-nitrobenzyl cyanide, and *p*-dimethylaminophenethylamine by Curtius degradation of β-*p*-dimethylaminophenylpropionic acid.[12]

The bisquaternary salts (I; R = R′ = R″ = Me; $n = 3$—5) were prepared from the appropriate 1-dimethylamino-ω-*p*-dimethylaminophenylalkanes. These were prepared by the general method (II—IV). The *n*-alkyl *p*-dimethylaminophenyl ketones (II; $n = 2$ and 3) were first synthesised in this way by Nineham [13] whose procedure was used for the homologues (II; $n = 4$ and 5). This work is included in the above publication,[13] together with proofs of the structure of the compounds (II; $n = 3$ and 4). The structure of the

$$p\text{-NMe}_2\cdot C_6H_5 + H\cdot[CH_2]_{n-1}\cdot CO_2H \xrightarrow{P_2O_5} p\text{-NMe}_2\cdot C_6H_4\cdot CO\cdot[CH_2]_{n-1}\cdot H \xrightarrow[-S]{NHMe_2}$$

(II)

$$p\text{-NMe}_2\cdot C_6H_4\cdot[CH_2]_{n-1}\cdot CS\cdot NMe_2 \xrightarrow{LiAlH_4} p\text{-NMe}_2\cdot C_6H_4\cdot[CH_2]_n\cdot NMe_2$$

(III) (IV)

(V) $p\text{-NH}_2\cdot C_6H_4\cdot[CH_2]_n\cdot NH_2$ $p\text{-NO}_2\cdot C_6H_4\cdot[CH_2]_{n-1}\cdot CN$ (VI)

ketone (II; $n = 5$) was established by hydrolysing the derived *NN*-dimethyl-δ-*p*-dimethylaminophenylthiovaleramide (III; $n = 5$) to the corresponding valeric acid, identical with that synthesised by standard methods from δ-*p*-nitrophenylvaleric acid.[14] The Kindler–Willgerodt reaction was used to convert the aldehyde (II; $n = 1$) and the ketones (II; $n = 2$—5) into the thioamides (III; $n = 1$—5). Malodorous, coloured, oily by-products were formed in increasing amounts on ascending the series, so that yields rapidly diminished (see Table 1) : the thioamides are however crystalline, and were isolated without undue difficulty even when the yield was as low as 5%. The thioamides (III; $n = 1$—5) were smoothly and efficiently converted into the diamines (IV; $n = 1$—5).

The bisquaternary salts (I; R = R′ = R″ = Me; $n = 3$—5) were prepared without difficulty from the amines (IV). The salt (I; R = R′ = R″ = Me; $n = 6$) was prepared by treating 6-*p*-aminophenylhexylamine with methyl iodide and sodium carbonate; the two homologues (I; R = R′ = R″ = Me; $n = 2$ and 3) were similarly prepared. The 4-alkylbenzene-1 : ω-bis(ethyldimethylammonium iodides) (I; R = R′ = Me, R″ = Et; $n = 1$—5) were prepared by treating the diamines (IV) with ethyl iodide, reaction being more sluggish than with methyl iodide.

[10] Shoppee, *J.*, 1931, 1237.
[11] Braun and Blessing, *Ber.*, 1923, **56**, 2160.
[12] Shoppee, *J.*, 1930, 968.
[13] Nineham, *J.*, 1952, 635.
[14] Plati, Strain, and Warren, *J. Amer. Chem. Soc.*, 1943, **65**, 1273.

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The 4-alkylbenzene-1 : ω-bis(triethylammonium iodides) (I; R = R′ = R″ = Et; *n* = 2—6) were prepared from the bisprimary amines (V), ethyl iodide, and sodium carbonate. The required ω-*p*-aminophenylalkylamines (V; *n* = 2—6) were obtained by

TABLE 1. ω-p-*Dimethylaminophenyl*-n-*alkane*-1-(NN-*dimethylthiocarboxyamides*) (III).

					Found (%)			Required (%)		
n − 1	Formula	Yield (%)	Form (solvent)	M. p.	C	H	N	C	H	N
0	$C_{11}H_{16}N_2S$	55	Needles (C_6H_6–Pet *)	105—106°	63·6	7·9	13·5	63·5	7·7	13·5
1	$C_{12}H_{18}N_2S$	20	Needles (EtOH)	102—103	64·9	8·1	12·5	64·9	8·1	12·6
2	$C_{13}H_{20}N_2S$	14	Plates (EtOH)	102—103	66·4	8·5	11·8	66·1	8·5	11·9
3	$C_{14}H_{22}N_2S$	5—7	Plates (EtOH)	83—84	67·2	9·0	11·1	67·2	8·8	11·2
4	$C_{15}H_{24}N_2S$	3—5	Plates (EtOH)	79	68·1	9·2	10·8	68·2	9·1	10·6

* Pet = light petroleum (b. p. 60—80°).

catalytic hydrogenation of the ω-*p*-nitrophenyl-*n*-alkyl cyanides (VI). The cyanides (VI; *n* = 2 and 3) were prepared by nitrating benzyl and 2-phenethyl cyanide, respectively; the latter nitration is described by Zemplen *et al.*,[15] the structure of their product now being proved by hydrolysis to the known acid.[16] The other homologous cyanides (VI; *n* = 4—6) were prepared from ω-*p*-nitrophenyl-butyric,[17] -valeric,[14] and -hexanoic acids.[17] With phosphorus pentachloride and then ammonia these acids yielded the amides which were converted into the cyanides by dehydration with thionyl chloride. In the preparation

TABLE 2. 1-*Dimethylamino*-ω-p-*dimethylaminophenylalkanes* (IV).

				Found (%)			Required (%)		
n	Formula	Yield (%)	B. p./mm.*	C	H	N	C	H	N
1	$C_{11}H_{18}N_2$	68	135°/15	73·8	10·1	15·5	74·2	10·1	15·7
2	$C_{12}H_{20}N_2$	86	146°/7	74·0	10·2	14·4	75·0	10·4	14·6
3	$C_{13}H_{22}N_2$	84	164°/15	73·5	10·9	13·4	75·7	10·7	13·6
4	$C_{14}H_{24}N_2$	72	182°/20	75·8	10·9	12·5	76·4	10·9	12·7
5	$C_{15}H_{26}N_2$	85	219°/33	77·3	10·8	11·9	76·9	11·1	12·0

* All the compounds are colourless or pale yellow, basic, water-soluble oils.

TABLE 3. ω-p-*Aminophenylalkylamines* (V).

		Yield	M. p. or	Found (%)				Required (%)		
n	Compound	(%)	b. p./mm.	C	H	N	Formula	C	H	N
3	Base [a]	80	179—182°/17							
	NN′-Ac_2 [b, c]		141—142	66·3	7·8	11·9	$C_{18}H_{18}O_2N_2$	66·7	7·7	12·0
	NN′-Bz_2 [b, d]		171—173	76·9	6·1	7·9	$C_{32}H_{32}O_2N_2$	77·1	6·2	7·8
4	Base [e]	63	176—178/13							
	NN′-Ac_2 [b, c]		154—155	67·6	8·2	10·9	$C_{14}H_{20}O_2N_2$	67·7	8·1	11·3
	NN′-Bz_2 [f, d]		224—225	77·2	6·5	7·7	$C_{34}H_{34}O_2N_2$	77·4	6·5	7·5
5	Base [e]	86	140—142/0·5							
	NN′-Bz_2 [e]		148—149°	77·7	6·8	7·3	$C_{35}H_{36}O_2N_2$	77·7	6·7	7·3
6	Base [g]	73	197—200/15							
	NN′-Ac_2 [g]		142	69·9	8·9	9·9	$C_{16}H_{24}O_2N_2$	69·6	8·7	10·2
	NN′-Bz_2 [b, d]		179—181	77·8	7·0	7·1	$C_{36}H_{38}O_2N_2$	78·0	7·0	7·0

[a] Cf. Müller, *Angew. Chem.*, 1949, **61**, 179; Patrick, McBee, and Hass, *J. Amer. Chem. Soc.*, 1946, **68**, 1153. [b] Needles. [c] From H_2O. [d] From EtOH. [e] Cryst. [f] Plates. [g] From aq. EtOH.

of the salt (I; R = R′ = R″ = Et; *n* = 2) the calculated quantity of sodium carbonate was used; reaction was much slower than in the corresponding trimethyl series. For the salts (I; R = R′ = R″ = Et; *n* = 3—6) it was essential to use 50% excess of sodium carbonate and to reflux the mixture until sodium carbonate was no longer present (50—100 hr.) to avoid contamination of the product with amine hydriodides. The compound

[15] Zemplen, Csürös, Gerecs, and Aczel, *Ber.*, 1928, **61**, 2491.
[16] Beilstein and Kuhlberg, *Annalen*, 1875, **163**, 132.
[17] Van der Scheer, *J. Amer. Chem. Soc.*, 1934, **56**, 744.

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(I; R = R′ = R″ = Et; *n* = 1) could not be prepared by treating *NN*-diethyl-4-diethylaminobenzylamine with ethyl iodide, only tetraethylammonium iodide being isolated from the gummy product.

TABLE 4. *4-Alkylbenzene-1 : ω-bis(trialkylammonium iodides)* (I).

						Found (%)			Required (%)	
n	R	R′	R″	Form	M. p.	N	I	Formula	N	I
0	Me	Me	Me	Plates [a]	>250°	6·1	56·2	$C_{12}H_{32}N_2I_2$	6·3	56·7
1	Me	Me	Me	Needles [a]	>250	6·1	54·8	$C_{13}H_{34}N_2I_2$	6·1	55·0
2	Me	Me	Me	— [b]	255	6·0	53·1	$C_{14}H_{36}N_2I_2$	5·9	53·4
3	Me	Me	Me	Needles [c]	175—180 *	5·6	51·9	$C_{15}H_{38}N_2I_2$	5·7	51·8
4	Me	Me	Me	— [c]	190—195	5·5	50·1	$C_{16}H_{40}N_2I_2$	5·6	50·4
5	Me	Me	Me	— [d]	~150 *	5·4	49·3	$C_{17}H_{42}N_2I_2$	5·4	49·0
6	Me	Me	Me	— [e]	~125 *	5·1	47·4	$C_{18}H_{44}N_2I_2$	5·3	47·7
2	Me	Me	Et	Needles [d]	200 *	5·5	50·9	$C_{16}H_{40}N_2I_2$	5·6	50·4
3	Me	Me	Et	— [d]	185 *	5·4	48·7	$C_{17}H_{42}N_2I_2$	5·4	49·0
4	Me	Me	Et	— [d]	155—158 *	5·2	47·4	$C_{18}H_{44}N_2I_2$	5·3	47·7
5	Me	Me	Et	— [f]	—	—	—	$C_{19}H_{46}N_2I_2$	—	—
2	Me	Et	Et	— [d]	190 *	5·4	47·7	$C_{18}H_{44}N_2I_2$	5·3	47·7
3	Me	Et	Et	— [d]	185 *	5·2	46·5	$C_{19}H_{46}N_2I_2$	5·1	46·5
4	Me	Et	Et	— [g]	176 *	5·0	45·5	$C_{20}H_{48}N_2I_2$	5·0	45·4
5	Me	Et	Et	— [f]	—	—	—	$C_{21}H_{50}N_2I_2$	—	—
2	Et	Et	Et	— [d]	187 *	5·1	45·3	$C_{20}H_{48}N_2I_2$	5·0	45·4
3	Et	Et	Et	— [h]	193 *	5·1	44·1	$C_{21}H_{50}N_2I_2$	4·9	44·3
4	Et	Et	Et	— [i]	~183 *	4·7	43·0	$C_{22}H_{52}N_2I_2$	4·8	43·2
5	Et	Et	Et	— [i]	—	4·4	41·0	$C_{23}H_{54}N_2I_2$	4·7	42·2
6	Et	Et	Et	— [h]	—	4·2	40·5	$C_{24}H_{56}N_2I_2$	4·6	41·2

* With decomp.

[a] From aq. EtOH. [b] From H_2O. [c] From MeOH. [d] From EtOH. [e] From MeOH–EtOH. [f] Gum, characterised as cryst. 4 : 4′-diaminostilbene-2 : 2′-disulphonate (cf. ref. 18). [g] From EtOH–$COMe_2$–EtOAc. [h] From EtOH–EtOAc. [i] From EtOH–$COMe_2$.

A glass was obtained on attempting to prepare the bisquaternary salt (I; R = Me, R′ = R″ = Et; *n* = 1) from 4-diethylamino-*NN*-diethylbenzylamine with methyl iodide. This diamine was obtained by lithium aluminium hydride reduction of the thioamide prepared by heating *p*-diethylaminobenzaldehyde with sulphur and diethylamine at 170°. For homologous thioamides similar routes were unsatisfactory, so required ω-diethylamino-1-*p*-diethylaminophenylalkanes were prepared by conversion of the iodides (I; R = R′ = R″ = Et; *n* = 2—5) into the chlorides which were distilled to give the crude diamines as colourless oils (contaminated with halogen-containing impurities) : the compounds were not obtained analytically pure but with methyl iodide furnished the desired bisquaternary salts (I; R = Me, R′ = R″ = Et; *n* = 2—6). The compounds where *n* = 2—4 were obtained crystalline, but those where *n* = 5 and 6 were gums. The product (*n* = 5) was converted into the crystalline 4 : 4′-diaminostilbene-2 : 2′-disulphonate.[18]

EXPERIMENTAL

Tetra-N-methyl-p-phenylenediamine.—*p*-Phenylenediamine (67 g.) was added gradually to stirred, ice-cooled 90% formic acid (200 c.c.) at 10—20°. The mixture was then warmed to 65° and 40% aqueous formaldehyde (280 c.c.) was added during 30 min. the temperature rising to 70°. Stirring was then stopped and the mixture heated at 88° (steam-bath) for 2 hr., cooled, basified with sodium hydroxide solution, and extracted with ether. The combined extracts were dried (Na_2SO_4) and fractionated. The fraction, b. p. 150—160°/27 mm. (9 g.), partly solidified and when drained gave the pale yellow ditertiary base (6 g., 5·5%), m. p. 50—51° (Meyer [7] gives m. p. 51°).

A solution of methyl iodide (50 c.c.) and the base (9·5 g.) in ethanol (125 c.c.) deposited during 30 min. *p*-dimethylaminophenyltrimethylammonium iodide (90%), m. p. *ca.* 265° (decomp.) (from aqueous ethanol) (Found : I, 41·7. Calc. for $C_{11}H_{19}N_2I$: I, 41·5%) (Pinnow and Pistov [8] give m. p. 265°). The crude iodide (12 g.) was heated with ethylene glycol (90 c.c.) and methyl iodide (30 c.c.) in a sealed tube at 100° for 72 hr. (heating for shorter periods gave a product

[18] Leeds and Slack, *J.*, 1956, 3941.

contaminated with the starting material). The resulting dark brown solid was freed from iodine by washing it with ethylene glycol, and distilling its solution in water with steam. The solution was then evaporated (15 mm.) to dryness, and the *p*-phenylene bis(trimethylammonium iodide) was triturated with acetone (see Table 4).

p-*Dimethylaminophenethylamine.*—β-*p*-Dimethylaminophenylpropionic acid [12] (7·5 g.), suspended in dry benzene (80 c.c.), was treated with thionyl chloride (15 c.c.) gradually with shaking. After 65 hr., the solvent and excess of thionyl chloride were evaporated at <30°/15 mm. The residue was dissolved in acetone (20 c.c.) and added during 10 min. to a stirred solution of sodium azide (5·2 g.) in water (40 c.c.) and acetone (15 c.c.) at 5—10°. Stirring was continued at room temperature for 15 min., and the mixture was extracted with benzene. The deep brown extracts were dried ($CaCl_2$), warmed on the steam-bath for 30 min., boiled for 1·5 hr. with concentrated hydrochloric acid (15 c.c.) and water (15 c.c.), and then evaporated to dryness (15 mm.). The dark semi-solid products from six such experiments were combined and dissolved in water, the solution was basified with sodium hydroxide solution and distilled with steam, and the distillate was acidified with hydrochloric acid and evaporated to dryness at 15 mm. The base was liberated from a concentrated solution of the dihydrochloride with solid sodium hydroxide and extraction with ether gave the amine (17·8 g., 47%), b. p. 152°/13 mm. The *N*-benzoyl derivative, crystallised in needles [from benzene–light petroleum (b. p. 80—100°)], m. p. 133° (Buck [19] gives m. p. 130°); the *phenylureido-derivative* formed plates (from ethanol), m. p. 158—159° (Found: C, 72·1; H, 7·4; N, 14·6. $C_{17}H_{21}ON_3$ requires C, 72·1; H, 7·4; N, 14·8%).

ω-p-*Nitrophenyl*-n-*alkane*-1-*carboxyamides.*—The ω-*p*-nitrophenyl-*n*-alkanoic acid [14,17] (0·2—0·4 mole), dissolved or suspended in dry benzene (500—1000 c.c.), was treated with phosphorus pentachloride (0·25—0·50 mole). After being kept at room temperature overnight, the resulting solution was gradually added to stirred, ice-cooled, concentrated aqueous ammonia (750—1500 c.c.) so that the temperature did not rise above 10°. Next day the crude carboxyamide was filtered off, washed with water, and dried. This material was used in preparations of the corresponding cyanides. Pure samples of the following carboxyamides were prepared: γ-p-*nitrophenylbutyramide* (75%), needles (from water), m. p. 135—137° (Found: C, 58·0; H, 6·0; N, 13·5. $C_{10}H_{12}O_3N_2$ requires C, 57·7; H, 5·8; N, 13·5%), δ-p-*nitrophenylvaleramide* (96%), slightly yellow needles (from benzene), m. p. 127—128° (Found: C, 59·6; H, 6·5; N, 12·5. $C_{11}H_{14}O_3N_2$ requires C, 59·5; H, 6·3; N, 12·6%), and 6-p-*nitrophenylhexanamide* (90%), pale yellow needles (from benzene), m. p. 120—122° (Found: C, 61·4; H, 6·8; N, 11·6. $C_{12}H_{16}O_3N_2$ requires C, 61·0; H, 6·8; N, 11·9%).

ω-p-*Nitrophenyl*-n-*alkyl Cyanides* (VI; $n = 1$—5).—The following were prepared by refluxing the appropriate amide (0·1—0·4 mole) with thionyl chloride (50—200 c.c.) for 2 hr. and fractionating the mixture: 3-p-*nitrophenylpropyl cyanide* (89%), b. p. 162—164°/0·5 mm. (Found: C, 63·0; H, 5·3; N, 15·0. $C_{10}H_{10}O_2N_2$ requires C, 63·2; H, 5·3; N, 14·7%), 4-p-*nitrophenylbutyl cyanide* (80%), yellowish rods (from ethanol), m. p. 43—44°, b. p. 188—190°/0·5 mm. (Found: C, 64·9; H, 6·0; N, 13·7. $C_{11}H_{12}O_2N_2$ requires C, 64·7; H, 5·9; N, 13·7%), and 5-p-*nitrophenylpentyl cyanide* (86%), b. p. 194°/0·5 mm. (Found: C, 66·0; H, 6·5; N, 13·0. $C_{12}H_{14}O_2N_2$ requires C, 66·1; H, 6·4; N, 12·8%).

2-*p*-Nitrophenethyl cyanide (VI; $n = 2$) was prepared by nitrating phenethyl cyanide (Henley and Turner [20]) as described by Zemplen *et al.*[15] Hydrolysis with boiling hydrochloric acid gave β-*p*-nitrophenylpropionic acid, m. p. 164° (Beilstein and Kuhlberg [16] give m. p. 163—164°).

4-p-*Aminophenylbutyl Cyanide.*—4-*p*-Nitrophenylbutyl cyanide (30 g.) in methanol (300 c.c.) was reduced with hydrogen at 30°/60 lb. per sq. in. in presence of Adams catalyst (2%) in 35 min. and afforded the new *cyanide* (18 g., 74%), b. p. 162—164°/0·5 mm. (Found: C, 75·5; H, 8·1; N, 16·2. $C_{11}H_{14}N_2$ requires C, 75·9; H, 8·1; N, 16·1%). The N-*benzoyl derivative*, platelets (from ethanol), had m. p. 145—146° (Found: C, 77·5; H, 6·5; N, 9·9. $C_{18}H_{18}ON_2$ requires C, 77·7; H, 6·5; N, 10·1%).

4-p-*Dimethylaminophenylbutyl Cyanide.*—A mixture of the above amino-nitrile (8·7 g., 0·05 mole), sodium carbonate (5·5 g., 0·055 mole), methyl iodide (20 c.c.), and methanol (50 c.c.) was refluxed for 3 hr. to give the required *cyanide* as a light yellow oil (6·8 g., 68%), b. p. 214—216°/20 mm. (Found: C, 77·1; H, 8·8; N, 13·9. $C_{13}H_{18}N_2$ requires C, 77·2; H, 8·9; N,

[19] Buck, *J. Amer. Chem. Soc.*, 1933, **55**, 2596.
[20] Henley and Turner, *J.*, 1931, 1183.

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13·9%). The yellow *picrate*, from ethanol, had m. p. 96—98° (Found: C, 52·5; H, 5·1; N, 16·0. $C_{19}H_{21}O_7N_5$ requires C, 52·9; H, 4·9; N, 16·2%).

δ-p-*Dimethylaminophenylvaleric Acid*.—(*a*) 4-*p*-Dimethylaminophenylbutyl cyanide (6 g.) with potassium hydroxide (6 g.) in ethanol (12 c.c.)–water (18 c.c.) at the b. p. (6 hr.) gave the *acid* (4·6 g., 70%), which crystallised from ethanol (charcoal) as a pinkish powder, m. p. 99—100° (Found: C, 71·0; H, 9·0; N, 6·3. $C_{13}H_{19}O_2N$ requires C, 70·6; H, 8·6; N, 6·3%). (*b*) A mixture of δ-*p*-dimethylaminophenyl-*NN*-dimethylthiovaleramide (1·7 g.), potassium hydroxide (2 g.), and water (20 c.c.) was refluxed for 10 hr., shaken with charcoal, and filtered, and adjusted to pH 6 by 2N-hydrochloric acid. The precipitated acid was dissolved in saturated aqueous sodium hydrogen carbonate, the turbid solution was shaken with charcoal and filtered, and 2N-hydrochloric acid was added to the filtrate to pH 6. The solution gradually deposited colourless needles (50 mg.) of the acid, m. p. 99—100°, identical with that prepared by method (*a*).

ω-p-*Dimethylaminophenyl*-n-*alkane*-1-(NN-*dimethylthiocarboxyamides*) (III; $n = 1$—5; Table 1).—A mixture of *p*-dimethylaminobenzaldehyde (or the appropriate *n*-alkyl *p*-dimethylaminophenyl ketone [13]) (0·2 mole), sulphur (6·4 g.), and anhydrous dimethylamine (12 c.c.) was heated in a thick-walled tube (12″ × 1″) at 170—180° (bath-temp.) for 3—4 hr. Crude thioamide (III; $n = 1$) was obtained as a dark solid which was purified by crystallisation. In the preparation of the amides (III; $n = 2$ and 3) the cold mixture was a dark brown, malodorous semi-solid mass. This was triturated with ether to give the crude product which was purified by crystallisation. In the case of products (III; $n = 4$ and 5) the mixture, a malodorous dark red oil, was dissolved in ether, the solution was extracted with insufficient 2N-hydrochloric acid to extract all the basic material, and the extracts were partly neutralised with dilute sodium carbonate. Resinous material was filtered off after addition of charcoal, and the filtrate was basified with sodium carbonate. The liberated dark oil was extracted with ether, and the extracts were shaken with charcoal and magnesium sulphate and then evaporated to dryness. The residual dark reddish-brown oil was triturated with ether at *ca.* −10° to yield the crude product which was purified by crystallisation.

1-ω-*Dimethylamino*-p-*dimethylaminophenylalkanes* (IV; $n = 1$—5; Table 2).—The appropiate thioamide (0·04—0·06 mole) in ether (500—1000 c.c.) was added during 30—60 min. to a stirred suspension of finely powdered lithium aluminium hydride (0·05—0·07 mole) in ether (100—150 c.c.). After the mixture had been stirred for a further 1 hr., water was added cautiously and the mixture treated with 2N-hydrochloric acid. The acid extracts were basified with aqueous sodium hydroxide and distilled with steam, and the bases were isolated as described for *p*-dimethylaminophenethylamine.

4-*Alkylbenzene*-1:ω-*bis*(*trimethylammonium Iodides*) (I; R = R′ = R″ = Me; $n = 0$—6; Table 4).—The compounds (I; $n = 3$—5) were prepared by treatment of the appropriate 1-dimethylamino-ω-*p*-dimethylaminophenylalkane (3—5 g.) in methanol (20—100 c.c.) with methyl iodide (10 c.c.). The compounds (I; $n = 1$ and 2) were prepared by adding methyl iodide (10 c.c.) to the 1-amino-ω-*p*-dimethylaminophenylalkane (0·1 mole) in methanol (50 c.c.). When the exothermic reaction had subsided the mixture was refluxed with sodium carbonate (10·6 g., 0·1 mole), methyl iodide (10 c.c.), and methanol (25 c.c.). The compound (I; $n = 6$) was prepared by boiling 6-*p*-aminophenylhexylamine (3·8 g., 0·02 mole) with methyl iodide (25 c.c.), sodium carbonate (4·6 g.; 0·044 mole) and methanol (100 c.c.) for 18 hr. The clear solution was evaporated at 15 mm., and the residual solid was triturated with acetone, giving the crude bisquaternary ammonium iodide. The compound (I; $n = 2$) was also prepared by gradually adding methyl iodide (300 c.c., 4·8 moles) to *p*-aminophenethylamine (54 g., 0·4 mole) and sodium carbonate (85 g., 0·8 mole) in methanol (750 c.c.). After the vigorous exothermic reaction had subsided the mixture was refluxed for 10 hr. The crude product (155 g., 80%) had m. p. 246—248° (decomp.). In all cases the compounds were purified by recrystallisation. The compound (I; $n = 3$) (66 g., 88%), m. p. *ca.* 175° (decomp.), was similarly prepared by refluxing 3-*p*-aminophenylpropylamine (23 g., 0·15 mole), sodium carbonate (35·2 g.; 0·31 mole), and methyl iodide (75 c.c.) in methanol (400 c.c.) for 7 hr.

4-*Alkylbenzene*-1:ω-*bis*(*ethyldimethylammonium Iodides*) (I; R = R′ = Me, R″ = Et; $n = 2$—5; Table 4).—The appropriate 1-dimethylamino-ω-*p*-dimethylaminophenylalkane (2·5—5·0 g.) in ethanol (10 c.c.) was refluxed with ethyl iodide (10 c.c.) for 2 hr. On cooling, only the compound (I; $n = 2$) separated in a form suitable for crystallisation. For the other compounds, the solvent and ethyl iodide were evaporated and the residual brown gum was

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triturated with acetone. Compounds (I; $n = 3$ and 4) were thus obtained crystalline and were purified by crystallisation, but compound (I; $n = 5$) was a gum which was converted into the 4 : 4′-diaminostilbene-2 : 2′-disulphonate as described in Part II.[18]

1-ω-p-*Aminophenylalkylamines* (V; $n = 2$—6) (Table 3).—The compounds were prepared by catalytic reduction of the nitro-cyanides (VI; $n = 1$—5) (0·15—0·40 mole) in methanol (150—400 c.c.) in the presence of Adams catalyst (2·5%) at 35°/70—80 lb. per sq. in. When reduction of the nitro-group was complete, the platinum was filtered off, anhydrous ammonia was introduced, and reduction of the cyano-group was effected in presence of Raney nickel (10%) at 55—70°/500—900 lb. per sq. in. After filtration and evaporation of the solvent, the residual oil was distilled, to give the diamine. The diamines distilled as colourless oils which crystallised and rapidly became brown in air. As they reacted readily with atmospheric carbon dioxide, the bases were not analysed but were characterised as their crystalline *NN*′-diacety and/or -dibenzoyl derivatives.

4-*Alkylbenzene*-1 : ω-*bis*(*triethylammonium Iodides*) (I; R = R′ = R″ = Et; $n = 2$—6; Table 4).—The compound (I; $n = 2$) was obtained on refluxing a mixture of *p*-aminophenethylamine (0·03 mole), sodium carbonate (6·4 g., 0·06 mole), ethanol (20 c.c.), and ethyl iodide (25 c.c.) for 20 hr. The clear solution, on cooling, deposited 4-ethylbenzene-1 : 2′-bis(triethylammonium iodide) which was recrystallised. When the compound (I; $n = 3$) was prepared in a similar way, the cooled reaction mixture was treated with acetone and kept at 0°. The solid, which separated, consisted of the bisquaternary salt mixed with amine hydriodides. The impurites were removed by repeated crystallisation from ethanol–ethyl acetate. Further quantities of the compound (I; $n = 3$) and of the compounds (I; $n = 4$—6) were prepared by refluxing the appropriate diamine (0·025—0·100 mole) with ethyl iodide (25—75 c.c.), ethanol (75 c.c.), and 50% excess of sodium carbonate (0·075—0·300 mole) until a clear solution was obtained (50—100 hr.). The solution was then evaporated at 15 mm. and the residual solid, which was sticky only in the case of compound (I; $n = 4$), was treated with acetone to yield the crude bisquaternary salt. In the preparation of the compounds (I; $n = 5$ and 6) the solid was completely soluble in acetone, but solid material was obtained on keeping the solution at 0° with or without the addition of ethyl acetate.

An attempt was made to prepare the compound (I; $n = 1$) by refluxing *NN*-diethyl-4-diethylaminobenzylamine (2·5 g.) with ethyl iodide (10 c.c.) for 24 hr. Ethanol and excess of ethyl iodide were evaporated and the residual brown gum was triturated with acetone (the acetone liquors yielded only gum), giving colourless crystals (1 g.), m. p. >260°. These were shown to be tetraethylammonium iodide (Found : I, 49·2. Calc. for $C_8H_{20}NI$: I, 49·4%) by conversion into the picrate, deep yellow needles (from ethanol), m. p. 248—249°, undepressed by mixing with an authentic sample, m. p. 251—252°.

4-*Diethylamino*-NN-*diethylbenzylamine*.—*p*-diethylaminobenzaldehyde (35·4 g., 0·2 mole), sulphur (6·4 g., 0·2 g.-atom), and diethylamine (14 c.c.) was heated at 170—180° for 3 hr. The *thioamide* was obtained as pale yellow platelets (11%), m. p. 86—88°, from light petroleum (b. p. 60—80°) (Found : C, 68·4; H, 9·1; N, 10·4. $C_{18}H_{24}N_2S$ requires C, 68·2; H, 9·1; N, 10·6%). Reduction with lithium aluminium hydride as described previously gave 4-*diethylamino*-NN-*diethylbenzylamine* (84%), b. p. 169°/7 mm. (Found : C, 76·9; H, 11·1; N, 11·5. $C_{15}H_{26}N_2$ requires C, 76·9; H, 11·1; N, 12·0%).

For the preparation of the other bisdiethylamino-compounds, the appropriate 1-*n*-alkylbenzene-4 : ω-bis(triethylammonium iodide) (0·01—0·07 mole) in water (250—1000 c.c.) was added to a stirred suspension of freshly prepared silver chloride (0·2 mole) in hot water (500 c.c.). The mixture was heated on the steam-bath and stirred for 2 hr., then filtered, and the combined filtrate and washings were shaken with charcoal. After removal of charcoal the filtrate was evaporated at 15 mm. and the residue of bisquaternary chloride was distilled *in vacuo*, to give the 1-diethylamino-ω-*p*-diethylaminophenylalkane. The products, after distillation, were contaminated with halogen-containing material (Beilstein test) and were not pure. The following were thus prepared : 1-diethylamino-2-*p*-diethylaminophenylethane (16%), b. p. 170—180° (bath-temp.)/17 mm., 1-diethylamino-3-*p*-diethylaminophenylpropane (29%), b. p. 194—196°/10 mm., 1-diethylamino-4-*p*-diethylaminophenylbutane (26%), b. p. 210—213° (bath-temp.)/10 mm., and 1-diethylamino-5-*p*-diethylaminophenylpentane (35%), b. p. 235—240° (bath-temp.)/18 mm.

4-*Alkylbenzene*-1 : ω-*bis*(*diethylmethylammonium Iodides*) (I; R = Me, R′ = R″ = Et; $n =$ 2—5; Table 4).—A solution of the 1-diethylamino-ω-*p*-diethylaminophenylalkane (2·5—4·5 g.)

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in methanol (10—20 c.c.) was refluxed with methyl iodide (10—15 c.c.) for 24 hr. Evaporation left a brownish gum. Trituration with acetone gave the crystalline compounds (I; $n = 2$—4) but the remaining gum would not solidify. This compound (I; $n = 5$) was converted into the 4 : 4′-diaminostilbene-2 : 2′-disulphonate as described in Part II.[18]

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THE RESEARCH LABORATORIES, MAY & BAKER, LTD.,
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523. *Synthetic Plant Hormones. Part V.* (+)- and (−)-2 : 4-Dichlorophenoxy-fluoro- and -difluoro-acetic Acid.*

By (MISS) M. H. MAGUIRE and G. SHAW.

(±)-2 : 4-Dichlorophenoxy-fluoro- and -difluoro-acetic acid have been prepared by reaction of sodium 2 : 4-dichlorophenoxide with ethyl chlorofluoroacetate and ethyl chlorodifluoroacetate respectively. The racemic monofluoro-acid was resolved with strychnine and (+)-α-methylphenethylamine.

SUBSTITUTION in the α-position of aryloxyacetic acids by alkyl groups has been shown to give compounds in which the growth-regulating properties are retained although sometimes modified,[1,2] and in which activity is governed by the stereochemical configuration.[3] In this series, enhanced activity is shown by the (+)-isomers whereas the (−)-enantiomorphs have negligible activity or may even possess anti-auxin properties. By contrast, αα-dialkyl derivatives are generally without growth-regulating properties, though exceptions are known.[2]

These results have been generalised in the so-called α-hydrogen effect,[2] the anomalies being ascribed to biological demethylation by a process such as $-CMe_2 \cdot CO_2H \longrightarrow -CMe(CO_2H)_2 \longrightarrow -CHMe \cdot CO_2H$. The inactivity of 2 : 4-dichlorophenoxymalonic acid[4] and the failure of biochemical experiments to support this scheme make it more attractive to postulate the scheme $-CMe_2 \cdot CO_2H \longrightarrow -CMe(CHO) \cdot CO_2H \longrightarrow -CHMe \cdot CHO \cdot \longrightarrow -CHMe \cdot CO_2H$. So we have prepared α-fluoro-derivatives of 2 : 4-dichlorophenoxyacetic acid since substitution of fluorine for hydrogen *in vivo* would be unlikely.

Sodium 2 : 4-dichlorophenoxide and ethyl chlorofluoroacetate in hot ethanol readily gave ethyl 2 : 4-dichlorophenoxyfluoroacetate and thence the acid, which was resolved into its optical enantiomorphs with strychnine and (+)-α-methylphenethylamine. The difluoro-acid was obtained with some difficulty by using ethyl chlorodifluoroacetate.

Preliminary biological tests by Mr. C. G. Greenham, Division of Plant Industry, C.S.I.R.O., Canberra; indicate that (+)-2 : 4-dichlorophenoxyfluoroacetic acid has pronounced auxin activity but less than that of 2 : 4-dichlorophenoxyacetic acid; the racemic acid has less and the (−)-isomer negligible activity. Incomplete tests of the

* Part IV, *J.*, 1957, 311.

[1] Wain, "Plant Growth Substances," Roy. Inst. Chem. Monograph, 1953; Fawcett, Osborne, Wain, and Walker, *Ann. Appl. Biol.*, 1953, **40**, 232.
[2] Fawcett, Wain, and Wightman, *Ann. Appl. Biol.*, 1955, **43**, 342.
[3] Smith, Wain, and Wightman, *ibid.*, 1952, **39**, 295.
[4] Cavill and Ford, *J.*, 1954, 1388.

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difluoro-acid indicate very slight auxin activity. These results appear to parallel the behaviour of the alkyl derivatives but it would be fallacious to draw further conclusions.

Experimental

Ethyl 2 : 4-*Dichlorophenoxyfluoroacetate.*—Ethyl chlorofluoroacetate was prepared from chlorotrifluoroethylene by reaction with ethanol and hydrolysis of the 2-chloro-1-ethoxy-1 : 1 : 2-trifluoroethane so formed;[5] the ester was kept over anhydrous potassium carbonate. Solutions of sodium (8·2 g.) in dry ethanol (80 ml.) were boiled with 2 : 4-dichlorophenol (58 g.) and ethyl chlorofluoroacetate (50 g.) in ethanol (300 ml.) for 2 hr., then kept for 4 days at room temperature. Sodium chloride was filtered off and washed with ethanol, and the filtrate evaporated to an oil which was added to water (300 ml.). An oil separated and was extracted with ether (4 × 50 ml.). The extract was washed with 4% sodium hydroxide solution (25 ml.) and water (6 × 10 ml.), then dried and evaporated to an oil (48 g.) which was distilled *in vacuo*, giving a low-boiling fraction (2 : 4-dichlorophenol) and then *ethyl* 2 : 4-*dichlorophenoxyfluoroacetate* (40·6 g.), b. p. 121—122°/1·5 mm., $n_D^{14\cdot5}$ 1·5108 (Found : C, 45·2; H, 3·5; Cl, 26·5. $C_{10}H_9O_3Cl_2F$ requires C, 44·95; H, 3·4; Cl, 26·5%). Positive tests for fluoride were obtained after sodium fusion.

The fluoro-ester (23·3 g.) in ethanol (15 ml.) was warmed with 10% sodium hydroxide solution (200 ml.). After a few minutes a crystalline salt separated. The mixture was kept overnight, and the salt (21 g.) filtered off, dissolved in water (150 ml.) and acidified with 10N-hydrochloric acid to precipitate the *acid* (15·2 g.), needles (from benzene–light petroleum), m. p. 91—93° (Found : C, 39·95; H, 2·15%; equiv., 239. $C_8H_5O_3Cl_2F$ requires C, 40·2; H, 2·1%; equiv., 239).

A suspension of strychnine (29·8 g.) in boiling acetone (250 ml.) was added to a warm solution of the racemic acid (21·35 g.) in acetone (100 ml.) and water (150 ml.). The clear solution obtained was boiled and filtered, then treated with hot water (400 ml.), cooled to room temperature, seeded, and kept for 2 days. The strychnine salt (58 g.) was filtered off and recrystallised 8 times from acetone–water (1 : 10). After each crystallisation a portion of the salt was decomposed with 7·5N-aqueous ammonia with warming. Strychnine was filtered off and the cooled filtrate acidified to precipitate the fluoro-acid which was recrystallised from *cyclo*hexane or benzene–light petroleum and the specific rotation determined. The (+)-*acid* was finally obtained as needles, m. p. 104—105°, $[\alpha]_D^{22\cdot5}$ +57·1° ± 0·3° * (*c* 1·505 in $CHCl_3$) (Found : C, 40·1; H, 1·95%).

A solution of (+)-α-methylphenethylamine (7·6 g.) in ether (100 ml.) was added to the racemic acid (13·8 g.) in ether (150 ml.); a crystalline salt separated. This was recrystallised 6 times from chloroform–ether. Portions were decomposed with 1·5N-sodium hydroxide, the base extracted with ether, and the fluoro-acid isolated as before. The (−)-*acid* separated from benzene–light petroleum as needles, m. p. 103—105°, $[\alpha]_D^{21\cdot5}$ −57·1° ± 0·3° (*c* 1·504 in $CHCl_3$) (Found : C, 40·2; H, 2·1%).

2 : 4-*Dichlorophenoxydifluoroacetic Acid.*—A mixture of dry sodium 2 : 4-dichlorophenoxide (25 g.) and ethyl chlorodifluoroacetate (54 g.) was boiled under reflux for 41 hr. The semisolid residue was stirred with ether (110 ml.) and 1% sodium hydroxide solution (100 ml.); unidentified crystals were filtered off and recrystallised from acetic acid as needles, m. p. 200—203° (Found : C, 47·6; H, 2·55%). The alkaline solution was acidified with 10N-hydrochloric acid and then extracted with ether. The ether solution was extracted with sodium hydrogen carbonate solution, and the solution acidified and re-extracted with ether. The dried solution was evaporated to an acidic oil which crystallised. 2 : 4-*Dichlorophenoxydifluoroacetic acid* (8·4 g.) separated from light petroleum as deliquescent needles, m. p. 68—71° (Found : C, 37·2; H, 1·5; Cl, 27·5. $C_8H_4O_3Cl_2F_2$ requires C, 37·4; H, 1·55; Cl, 27·6%). A solution in ether gave the p-*toluidine salt*, plates (from ethyl acetate–*cyclo*hexane), m. p. 134—135° (Found : C, 49·5; H, 3·8; N, 3·85. $C_8H_4O_3Cl_2F_2,C_7H_9N$ requires C, 49·45; H, 3·6; N, 3·85%).

The acid (0·73 g.) in ethanol (5 ml.) was boiled for 1 hr., then kept at room temperature for

* Limits of error in optical rotations were calculated by use of formulæ (±) $3\Sigma x/(n\sqrt{n})$ and (±) $0{\cdot}6745\sqrt{(\Sigma x^2/n)}$ where x is the residual and n the number (10) of readings.

[5] Young and Tarrant, *J. Amer. Chem. Soc.*, 1949, **71**, 2432; *Org. Synth.*, 1954, **34**, 49.

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3 days. The solvent was removed and the residue dissolved in dry ether, dried (K_2CO_3), evaporated, and distilled, giving the *ethyl ester* (0·49 g.), b. p. 80—88°/0·5 mm., $n_D^{22\cdot5}$ 1·4833 (Found: C, 41·9; H, 2·85. $C_{10}H_8O_3Cl_2F_2$ requires C, 42·15; H, 2·85).

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524. *Infrared Spectra and the Polymorphism of Glycerides. Part III.*[1] *Palmitodistearins and Dipalmitostearins.*

By D. Chapman.

Polymorphism of the palmitodistearins and dipalmitostearins has been investigated by means of infrared spectroscopy between 1800 and 650 cm.$^{-1}$. The transitions have been studied and the packing of the chains deduced.

In previous papers [1] it was deduced that the lowest-melting form of a triglyceride was an α-form with hexagonal packed chains rather than a vitreous form, whilst the next-highest-melting form designated α by Malkin [2] was almost certainly not a form with hexagonal packing of the hydrocarbon chains and was thus wrongly designated. These views support the conclusions by American workers [3] from *X*-ray evidence. The present paper extends the infrared spectroscopic study to the polymorphism of 1-palmitodistearin (PSS), 1-stearodipalmitin (SPP), 2-palmitodistearin (SPS), and 2-stearodipalmitin (PSP). Controversy about these glycerides concerns the association of *X*-ray data with melting points, the existence of certain polymorphic forms,[4] and the nomenclature. The last becomes important here, since the stable form of PSP, about which there is agreement over the melting point and *X*-ray data, is designated a β′-form by Lutton *et al.*[4] but a β-form by Malkin.[2]

Experimental

2-Palmitodistearin, m. p. 67·3°, 2-stearodipalmitin, m. p. 67·5°, 1-palmitodistearin, m. p. 65·0°, and 1-stearodipalmitin, m. p. 62·5°, were prepared by Dr. W. T. Weller of this laboratory by hydrogenation of the disaturated oleo-glycerides [5] at room temperature in the presence of palladised charcoal in ethyl acetate, followed by recrystallisations from solvents.

The infrared spectrometer was a Grubb-Parsons S3 double-beam spectrometer with a rock-salt prism. The spectra were in general obtained between 1800 and 650 cm.$^{-1}$ with capillary thicknesses of the glycerides between rock-salt flats. An infrared cell which could be heated or cooled was used for the investigation of the liquid and for the polymorphic transitions which occur on heating or cooling. Rapid scanning of parts of the spectrum (in particular the 720 cm.$^{-1}$ and the 1250 cm.$^{-1}$ region) during heating or cooling disclosed the transition temperatures. These were confirmed by capillary-tube methods (cf. Lutton *et al.*). The forms obtained by crystallisation from solvent were examined both as Nujol mulls and in potassium bromide discs. The identities of the stable forms were confirmed by m. p. and *X*-ray data.

Results and Discussion

Infrared spectra (see Fig. 1) show three polymorphic forms of 1-palmitodistearin (PSS). The lowest-melting form was obtained by quenching the liquid to 0°; its spectrum is

[1] Parts I and II, Chapman, *J.*, 1956, **55**, 2522.
[2] Malkin, "Progress in Chemistry of Fats and Other Lipids," Vol. II, Pergamon Press Ltd., London, 1954.
[3] Bailey, Jefferson, Kreeger, and Bauer, *Oil and Soap*, 1945, **22**, 10; Filer, Sidhu, Daubert, and Longenecker, *J. Amer. Chem. Soc.*, 1946, **68**, 167; Lutton, *ibid.*, 1945, **67**, 524.
[4] Malkin and Meara, *J.*, 1939, 103; Carter and Malkin, *J.*, 1939, 577; Lutton, Jackson, and Quimby, *J. Amer. Chem. Soc.*, 1948, **70**, 2441.
[5] Chapman, Crossley, and Davies, *J.*, 1957, 1502.

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similar in general to that of the α-form of tristearin,[1] and is similarly designated: in particular there is a single component of the methylene rocking mode at 720 cm.$^{-1}$. When this form was heated and the spectrum rapidly scanned, a transition was noted to occur at 50·5° to an intermediate-melting form. This behaviour is different from that of the simple saturated triglycerides such as tristearin, where direct transformation from the α- to the β-form occurs.[1] The spectrum of the intermediate form is in general very similar to that of the β′-form of tristearin and is therefore designated a β′-form: in particular there are two components of the band assigned to a methylene rocking mode at 719 and 720 cm.$^{-1}$. The bands in the 1250 cm.$^{-1}$ region are not quite as well resolved as those in tristearin. When further heated, this form melted at 61·5°. (This intermediate form was also obtained by crystallisation from ethyl acetate.) The highest-melting form was obtained by slow crystallisation from acetone: its spectrum is similar in general to that of the β-form spectrum of tristearin and is similarly designated; in particular, there is a prominent band at 890 cm.$^{-1}$ and a single component of the methylene rocking mode at 717 cm.$^{-1}$. These bands are characteristic [2] of the β-forms of tristearin, tripalmitin, and trilaurin. The three forms show a marked change in the intensities of the bands in the 1250 cm.$^{-1}$ region. The spectrum of the β-form shows a pronounced band at 1268 cm.$^{-1}$ with weaker bands round it (perhaps arising from methylene wagging or twisting modes [1]). A similar argument to that used to designate the spectra of the polymorphic forms of tristearin [1] can also be applied to the spectra of this glyceride.

The infrared spectra (Fig. 2) show three forms of 1-stearodipalmitin (SPP). The lowest-melting form was obtained by quenching the liquid to 0°, and its spectrum is similar in general to that of the α-form of tripalmitin and is similarly designated: in particular there is a single component of the rocking mode at 720 cm.$^{-1}$. Heating and rapid scanning shows a transition to an intermediate-melting form at 47°, whose spectrum is in general similar to that of the β′-form of tripalmitin [1] and is similarly designated: its methylene rocking mode consists of a doublet at 728 and 718 cm.$^{-1}$. This form is transformed at 57° into a more stable form which is also obtained by slow crystallisation from acetone. The spectrum of this form is very similar to that of the β-form of tripalmitin. The spectra of the three forms of SPP resemble those of PSS in the 1250 cm.$^{-1}$ region.

This work confirms the conclusions by Lutton *et al.*[4] (based on *X*-ray evidence and thermal data) that these glycerides can exist in α-, β′-, and β-forms.

Infrared spectra (Fig. 3) reveal only two forms of 2-palmitodistearin (SPS). The lower-melting form was obtained by quenching to 0° and its spectrum is similar in general (with some slight shifts in frequency of bands in the 1250 cm.$^{-1}$ region) to that of the α-form of tristearin and is similarly designated. Heating and scanning showed a transition at 50·5° to a more stable form whose spectrum was in general similar to that of the β-forms of other glycerides and is designated β: in particular there is a band at 890 cm.$^{-1}$ and a single band at 717 cm.$^{-1}$. (The spectrum of the stable crystalline form from solvent was identical with this.) The intensity pattern of the bands in the 1250 cm.$^{-1}$ region, although in general similar to that of the spectrum of the β-form of other glycerides, is a little different from that of SPP or tristearin (see Fig. 4): two bands near 1256 and 1268 cm.$^{-1}$ are of comparable intensity. Since attempts to obtain an intermediate form giving a spectrum similar to that obtained with other β′-forms failed, it must be of a fleeting nature if it exists. This can be compared with the conclusions by Lutton *et al.*[4] (based on *X*-ray evidence) and by Crowe and Smyth [6] (based on dielectric measurements) that only two forms exist for this glyceride, but Malkin and Meara [4] claim the existence of four forms and give *X*-ray data for a β′-form.

The infrared spectra (Fig. 4) also reveal only two forms of 2-stearodipalmitin (PSP). This also agrees with the conclusions by Lutton *et al.*[4], although Malkin and Meara [4] claim four forms also for this glyceride. The lower-melting form was obtained by quenching the

[6] Crowe and Smyth, *J. Amer. Chem. Soc.*, 1951, **73**, 2040.

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FIG. 1. 1-*Palmitodistearin* (*for* α_L *etc., see p.* 2719).

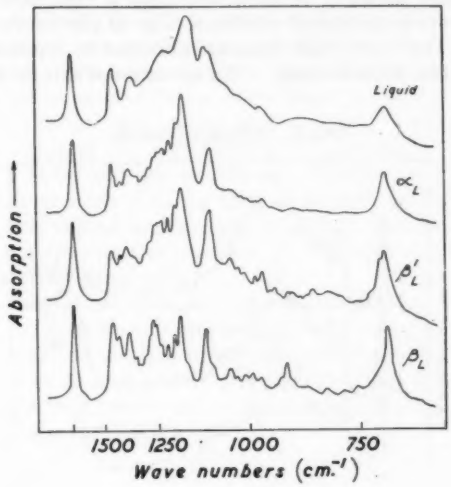
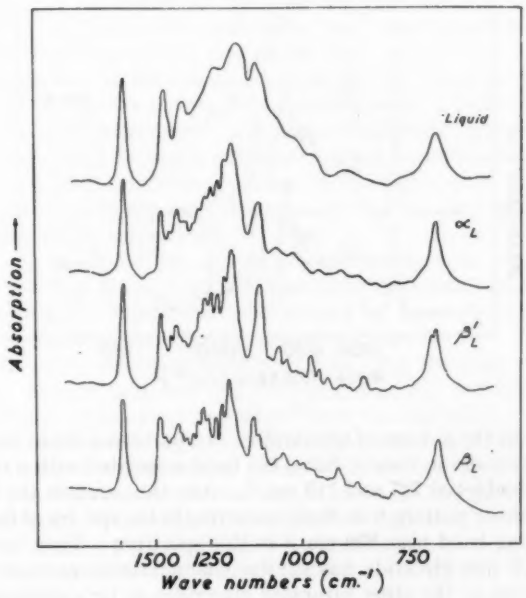


FIG. 2. 1-*Stearodipalmitin*.



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liquid to 0°, but was unusually unstable (cf. Lutton *et al.*, and Crowe and Smyth) in contrast to the stability of the α-form of SPS (the transition temperature for this form was obtained only by the capillary-tube thrust-in method), and made it difficult to obtain a satisfactory spectrum. The spectrum is in general similar to that of the α-form of tripalmitin and is similarly designated. The more stable form was obtained by crystallisation from the melt and by slow crystallisation from acetone. The spectrum of this form is similar to, but not

FIG. 3. *2-Palmitodistearin.*

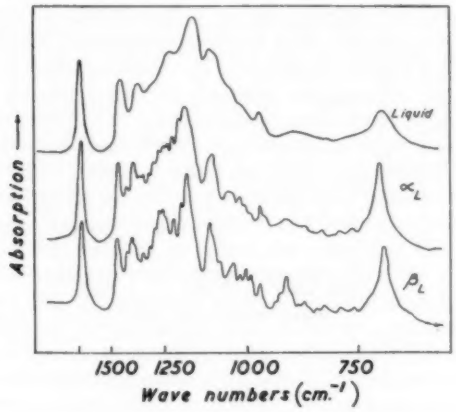
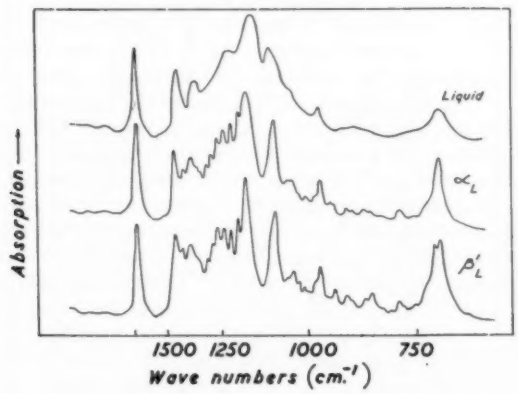


FIG. 4. *2-Stearodipalmitin.*



identical with, that of the β′-form of tripalmitin. In particular (as in the spectra of other simple saturated glycerides in their β′-form) the band associated with a methylene rocking mode consists of a doublet at 727 and 719 cm.$^{-1}$. Also the bands in the 1250 cm.$^{-1}$ region have a different intensity pattern from those occurring in the spectra of forms designated β, and there is no strong band near 890 cm.$^{-1}$ in this spectrum. That the spectrum of the most stable form of this glyceride has similar characteristics to those associated with spectra of the β′-forms of the other saturated glycerides so far examined is of particular interest.

In the first place there can be little doubt that this is the spectrum of a homogeneous

form since it was obtained by very slow crystallisation from solvent, confirming the view that the similar spectra of the β′-forms of other triglycerides which have been obtained by thermal treatment (*e.g.*, that of tristearin, PSS, etc.) are also those of essentially homogeneous forms. Secondly, its *X*-ray pattern shows that it is not an α-form (it has in fact been noted [2] that the *X*-ray short spacings of this form are practically identical with those of the β′-forms of simple odd-acid glycerides of the same acyl length). Yet the characteritics of this spectrum are the same as those given by the forms of tristearin, tripalmitin, 1-stearodipalmitin, etc., which Malkin would designate as α-forms. The inconsistency further supports the arguments given previously [1] that these forms are correctly assigned as β′-forms and not as α-forms. Malkin and Meara [4] in fact designate this form of PSP a β-form since it is the form of highest melting point, whilst Lutton *et al.*,[4] using a nomenclature based on *X*-ray short spacings, designates this a β′-form. The general similarity of the spectrum of this form to the spectra of the β′-forms of other glycerides supports the latter designation.

The existence of two systems of nomenclature, one based on melting points and the other on *X*-ray data, to describe the polymorphic forms of glycerides is confusing. A possible compromise to aid clarification would be to use the suffix M and L (M for Malkin and L for Lutton) in order to give a more precise designation of a particular form. The stable form of PSP could then be referred to as either a β_M- or a β'_L-form. (This suffix is used in the present Figures and Table.)

	PSS	SPP	SPS	PSP
α_L	50·5°	47°	50·5°	47°
β'_L	61·5°	57°	—	67·5°
β_L	65·0°	62·5°	67·3°	—

The melting point and transition data for the palmitic-stearic glycerides (see Table) agree well with those of Lutton *et al.*[4]

It is now possible to reconsider the basis for the polymorphism of the saturated triglycerides, by considering permissible deductions from infared spectra and supplementing them with published conclusions from *X*-ray evidence.

Saturated triglycerides so far examined show spectra corresponding to three polymorphic forms. All the spectra show a carbonyl absorption at 1730—1740 cm.$^{-1}$ and two strong bands near 1170 and 1100 cm.$^{-1}$. The major distinctions between the spectra of the different forms occur in the 1250 and the 720 cm.$^{-1}$ region (other bands in the region 1100—720 cm.$^{-1}$ are nevertheless distinctive). Bands in these two main regions are generally associated with vibrations of the methylene groups, and in particular with wagging (or twisting) and rocking modes respectively.[7]

A comparison of the spectrum of the lowest-melting form (α_L) of the saturated triglycerides with the type of spectrum obtained from the α-forms of alcohols, esters, and hydrocarbons supports the conclusion (also arrived at from the *X*-ray short spacing) that in this form the chains are hexagonally packed (cf. Part 2).

In the spectrum of the next-highest-melting form (β'_L) the band associated with the methylene rocking mode is split into two components at 727 and 719 cm.$^{-1}$. This is of particular significance. It has been suggested [8] that the existence of a similar doublet in the spectrum of orthorhombic and monoclinic hydrocarbons arises from interactions between adjacent chains in the crystalline phase, which result in an in-phase and an out-of-phase rocking mode. This doublet is observed, however, in the spectra of the crystalline form of many long-chain compounds, and Chapman [9] suggested that it is usually observed when orthorhombic packing of the hydrocarbon chain occurs, owing to similar interaction in the sub-cell. The doublet in the 720 cm.$^{-1}$ region in the spectra of the β'_L-form of the

[7] Brown, Sheppard, and Simpson, *Phil. Trans.*, 1954, **247**, 35.
[8] Stein, *J. Chem. Phys.*, 1955, **23**, 734.
[9] Chapman, 6th Internat. Spectroscopic Colloquium, Amsterdam, May, 1956.

triglycerides suggests that the hydrocarbon chains in this form are packed in the orthorhombic manner.

In the spectrum of the β_L-form of the triglycerides the band associated with the methylene rocking mode is single and at 717 cm.$^{-1}$. We deduce that in this form the hydrocarbon chains are probably not orthorhombically packed. An *X*-ray single-crystal structure determination [10] of the stable β_L-trilaurin shows that the hydrocarbon chains in this form have triclinic packing.

In this way we have essentially classified the polymorphic forms of the simple saturated triglycerides into three crystallographic types according to their hydrocarbon-chain packing or, in other words, according to the symmetry of their sub-cells. It is well known that long-chain crystals can be thus described.[11] Thus the α_L-form has hexagonal sub-cell symmetry, the β'_L-form orthorhombic sub-cell symmetry, and the β_L-form triclinic sub-cell symmetry. This throws light on to the classification of triglycerides by means of their *X*-ray short spacings proposed by Lutton,[12] since with long-chain compounds the short spacings will be determined primarily by the packing of the hydrocarbon chains. The short-spacing classification is therefore possible because of the underlying symmetry of the sub-cell.

Malkin [2] recently criticised the short-spacing classification on the grounds that all the β_M-forms of certain glycerides give the 3·8 and 4·2 Å lines. On the present view this means only that the stable form of these glycerides has orthorhombic packed chains. Other long-chain compounds show somewhat similar variation in the packing of the chains in their stable form: *e.g.*, the stable crystalline form for monocarboxylic acids of less than 22 carbon atoms has triclinic packed chains, whilst for molecules of longer chain length the stable form has orthorhombic packed chains.[13] A further criticism [2] that both β'_M- and β_M-forms of 1 : 3-diglycerides show the 4·6 Å line is explained if one argues that both these forms have triclinic packing of the chains and differ only in their tilt.

Lutton's classification extended to 1-monoglycerides [14] leads to a designation sub-alpha. (The *X*-ray short spacings of this form are very similar to those of the β′-form.) The spectrum of the sub-alpha form [1] shows a doublet at 719 and 727 cm.$^{-1}$, which suggests that the chains in this form are orthorhombically packed. The β′-form of 1-monoglycerides, *e.g.*, 1-monostearin, was considered [1] to have only a single band at 719 cm.$^{-1}$ (an additional band occasionally observed at 727 cm.$^{-1}$ with some samples was attributed to the presence of some sub-alpha form). This conclusion however is incorrect, and re-examination of the spectrum of this form shows that the β′-form also has a doublet at 727 and 719 cm.$^{-1}$ (cf. the β′-form spectrum of 1-monostearin [15]). This suggests that there are two closely related forms with orthorhombic packed chains in 1-monoglycerides.

We can conclude that for the glycerides so far examined the infrared spectra show Lutton's short-spacing classification to be reasonable and useful and to be based on sub-cell symmetry. Distortions from the strictly orthorhombic or triclinic type packing are possible, however, which could affect the short spacings, so that caution is needed about its overall generality (cf. Filer *et al.*[16] on an apparent anomaly with 1-stearyl 2-acyl 3-decanoyl glycerides).

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[10] Vand and Bell, *Acta Cryst.*, 1951, **4**, 465.
[11] Daniel, *Adv. Physics*, 1953, **2**, 457.
[12] Lutton, *J. Amer. Oil Chem. Soc.*, 1950, **27**, 276.
[13] Von Sydow, *Arkiv Kemi*, 1956, **9**, 231.
[14] Lutton and Jackson, *J. Amer. Chem. Soc.*, 1948, **70**, 2445.
[15] Chapman, *Nature*, 1955, **176**, 216.
[16] Filer, Sidhu, Chen, and Daubert, *J. Amer. Chem. Soc.*, 1945, **67**, 2085.

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525. *The Isolation and Constitution of Mollisacacidin, a New* leuco*Anthocyanidin from the Heartwood of* Acacia mollisima *Willd.*

By H. H. Keppler.

A new *leuco*anthocyanidin, mollisacacidin, has been isolated from the heartwood of *Acacia mollisima* (black wattle). Oxidation by periodic acid of its trimethyl ether revealed the presence of a glycol group, which is shown to be *cis*. With potassium permanganate in acetone this ether yielded 4-methoxysalicylic and veratric acid. The structure of the *leuco*anthocyanidin is thus postulated as *cis*-3 : 4 : 7 : 3′ : 4′-pentahydroxyflavan, which is confirmed by reduction of fustin (isolated from the heartwood of *Rhus glabra*) to mollisacacidin. The natural and synthetic *leuco*anthocyanidin both give fisetinidin chloride on treatment with mineral acid.

The first reported isolation of a crystalline *leuco*anthocyanin from a natural source was the recent instance of one from *Acacia mollisima* (black wattle).[1] King and Bottomley [2] obtained an amorphous *leuco*anthocyanidin from *Acacia melanoxylon*, but fully characterised the compound with crystalline derivatives. In the present investigation, black wattle heartwood was extracted with hot acetone. A light brown fraction therefrom, soluble in hot water and in cold acetone, was polyphenolic since it gave a green colour with ferric chloride. Two-dimensional paper chromatography disclosed two main components. Column chromatography on Solka-floc (B.W. 200 grade) with water as developer yielded two compounds giving characteristic *leuco*anthocyanidin tests;[3] one (in small yield) was amorphous; the other crystallised and is named mollisacacidin. The amorphous *leuco*anthocyanidine had the same R_F as (+)-catechin, but had absorption maxima at 280 and 310 mμ whereas catechin had only one (280 mμ): the crystalline *leuco*anthocyanidin had maxima at 230 and 280 mμ. Both *leuco*anthocyanidins are non-glycosidic, and both are converted into the same anthocyanidin, R_F 0·69, by 10% ethanolic hydrochloric acid. It is considered that the amorphous compound may be a polymer of the crystalline monomer. With methyl sulphate and potassium carbonate in acetone or with diazomethane, mollisacacidin gave a crystalline trimethyl ether, and with acetic anhydride a penta-acetate. It thus contains five hydroxyl groups, three of them phenolic. Mitchell's colorimetric method [4] showed the presence of two *ortho*-phenolic hydroxyl groups.

Periodic acid at room temperature rapidly oxidised mollisacacidin trimethyl ether, two equivalents of oxygen being consumed. An αβ-glycol structure is thus shown, and the *cis*-configuration was indicated by formation of an acidic borate complex by the methylated *leuco*anthocyanidin with sodium borate.[5] With potassium permanganate, mollisacacidin trimethyl ether gave 4-methoxysalicylic and veratric acid, identified by m. p.s and infra-red spectra over the skeletal range 700—1700 cm.$^{-1}$.

The structure as *cis*-3 : 4 : 7 : 3′ : 4′-pentahydroxyflavan was then conclusively proved by catalytic conversion of fustin (3 : 7 : 3′ : 4′-tetrahydroxyflavanone), isolated from the heartwood of *Rhus glabra*, into mollisacacidin. Catalytic reduction of this type of compound should favour formation of the *cis*-glycol.[6] Further, both the natural and the synthetic *leuco*anthocyanidin gave fisetinidin chloride [7] on treatment with 3N-hydrochloric acid in hot propan-2-ol.[8] Whereas several solvent systems failed to differentiate between fisetinidin and pelargonidin chloride on paper chromatography, Geissman and Jurd's

[1] Keppler, *Chem. and Ind.*, 1956, 380.
[2] King and Bottomley, *ibid.*, 1953, 1368; *J.*, 1954, 1399.
[3] Bate-Smith, *Biochem. J.*, 1954, **58**, 122.
[4] Mitchell, *Analyst*, 1923, **48**, 2; 1924, **49**, 162; *J. Internat. Soc. Leather Trades' Chemists*, 1936, **20**, 99.
[5] Boëseken and Hermans, *Rec. Trav. chim.*, 1921, **40**, 525.
[6] Joshi and Kulkarni, *Chem. and Ind.*, 1954, 1456; *J.*, 1953, 1027; Hückel, *Annalen*, 1937, **533**, 1.
[7] Freudenberg and Maitland, *Annalen*, 1934, **510**, 193.
[8] Hillis, *J. Internat. Soc. Leather Trades' Chemists*, 1954, **38**, 91.

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spectrographic method[9] achieved this; it is based on the ability of anthocyanidins having adjacent phenolic hydroxyl groups to form a complex with aluminium in neutral solution.

A second fraction of the crude extract contained pinitol, an inositol methyl ether previously found in wattle wood by Stephen [10] and a common constituent of conifers.[11] A third fraction yielded a crystalline compound agreeing in analysis with the steroid isolated by Stephen [10] from wattle wood but differing from it in its Liebermann–Burchard colour reaction and in the analysis of its monoacetate.

Experimental

Extraction of Heartwood.—Air-dried ground wattle heartwood (2 kg.) was extracted with acetone (4 l.) under reflux for 4 hr. After three extractions, the combined filtrates were evaporated at 50° under a reduced pressure of nitrogen. The dark brown residue was fractionated by repeated extraction with hot water. Insoluble material (A) was set aside. The solution of the water-soluble material (B) was evaporated at 80° under a reduced pressure of nitrogen, giving a dark brown powder (25 g.). This was triturated with cold anhydrous acetone; the soluble material was isolated as above and comprised fraction I. Acetone-insoluble material comprised fraction II. The water-insoluble material (A) was extracted (Soxhlet) with ether (500 ml.) for 6 hr. The yellow ethereal solution was evaporated under reduced pressure to give a light yellow residue (fraction III).

Fraction I.—(a) *Paper chromatography.* A portion (0·1 g.) in acetone (5 ml.) was chromatographed on Whatman's No. 2 paper, with aqueous 6% acetic acid as the one-way developer. The developed chromatogram was dried and dipped in 1 : 1 aqueous 0·3% ferric chloride and 0·3% potassium ferricyanide. Apart from a certain degree of trailing from the origin of the chromatogram, two compounds, R_F 0·65 and 0·53, staining blue, were revealed.

(b) *Separation of the components.* " Solka-floc " in 6% aqueous acetic acid was placed in a Pyrex-glass column (2" × 36"), and after settling was washed with 6% aqueous acetic acid, and then with distilled water until free from acid. Fraction I (16 g.) in cold water (40 ml.) was added and the column developed with water; " break through " of phenolic material was found by the ferric chloride–ferricyanide reagent. The fractions were collected and analysed on paper as above. Fractions 1—3 contained no polyphenols. Fractions 4—5 contained a phenol of R_F 0·64, and fractions 6—8 contained this phenol and another, of R_F 0·53. Fractions 9 and 10 contained only traces thereof.

Fractions 4—8 were combined and evaporated at 50° under a reduced pressure of nitrogen to 20 ml., then chromatographed as previously, but on a smaller column. The two compounds, R_F 0·64 and 0·53, were thus completely separated.

(c) *Compound, R_F 0·53.* The appropriate solutions were evaporated to 15 ml. No crystallisation occurred, even after 72 hr. Evaporation to dryness at 50° as above gave a light brown powder.

(d) *Mollisacacidin, R_F 0·64.* The combined solutions containing this compound were evaporated to 20 ml. and crystallised after 24 hr. The colourless *compound* was recrystallised several times from hot distilled water, colourless needles being obtained. The purified material gradually reddens above 110°, melts indefinitely at 125—130°, and has $[\alpha]_D^{18}$ 12·6° (*c* 1 in MeOH), $\lambda_{max.}$ 230, 280 mμ (log ε 4·26, 3·83), $\lambda_{min.}$ 254 mμ (log ε 2·92) (Found, in a sample dried at 56°/0·2 mm.: C, 55·5; H, 5·7. $C_{15}H_{14}O_6.2H_2O$ requires C, 55·2; H, 5·5%).

Methylation of Mollisacacidin.—(*a*) Mollisacacidin (1·5 g.) and diazomethane (from nitrosomethylurea, 20 g.) in methanol (100 ml.) were kept at 0° for 24 hr., then treated with acetic acid, and evaporated under reduced pressure. The residue, in ether, was washed with 4% aqueous sodium hydroxide and then water, and evaporated to an almost colourless residue (1·2 g.). Recrystallisation of this from ether–light petroleum (b. p. 40—60°) afforded the *ether* as needles. m. p. 129° (sinter 76—77°) [Found, in a sample dried at 65°/0·2 mm.: C, 64·4; H, 6·3; OMe, 27·0%; *M* (Rast), 337. $C_{18}H_{20}O_6$ requires C, 65·0; H, 6·1; 3OMe, 28·0%; *M*, 332].

(*b*) To mollisacacidin (0·5 g.) in anhydrous acetone (70 ml.), containing anhydrous potassium

[9] Geissman and Jurd, *Arch. Biochem. Biophys.*, 1955, **56**, 259.
[10] Stephen, *J. Sci. Food Agric.*, 1952, **3**, 37.
[11] Plouvier, *Compt. rend.*, 1953, **236**, 317.

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hydrogen carbonate (7 g.), dimethyl sulphate (1·5 ml.) was gradually added with stirring. The whole was heated on a water-bath for 4 hr., filtered, and evaporated under reduced pressure. The yellow residue was treated in benzene with charcoal and stirred into an excess of light petroleum (b. p. 40—60°). The white flocculent precipitate recrystallised from ether as needles (130 mg.), m. p. 128—130° alone or mixed with the material from (*a*).

Acetylation of Mollisacacidin.—Mollisacacidin (200 mg.), pyridine (3 ml.), and acetic anhydride (2 ml.) were kept overnight at room temperature, then heated on a water-bath for 15 min. and poured into an excess of cold water. The precipitated *acetate* was repeatedly dissolved in ether and reprecipitated with light petroleum (Found, in a sample dried at 100°/0·2 mm.: C, 60·0; H, 5·1; Ac, 42·2. $C_{25}H_{34}O_{11}$ requires C, 60·0; H, 4·8; Ac, 43·0%).

The Glycol Group.—Mollisacacidin trimethyl ether (34·6 mg.) and catechin tetramethyl ether (35·5 mg.) were dissolved separately in methanol (50 ml.). To each, in turn, were added 2 ml. of 0·5M-periodic acid and each whole diluted to 100 ml. A control (100 ml.), of 2 ml. of 0·5M-periodic acid in methanol, was also prepared. Aliquot parts (10 ml.) were withdrawn at intervals. Before titration, cold saturated sodium hydrogen carbonate solution (5 ml.) was added. The iodine liberated on addition of potassium iodide was titrated against 0·01N-arsenious oxide. After 2·5 hr. 1·02 mols. of periodate were consumed, but this gradually increased, being 1·09 mols. after 20 hr. There was no absorption with catechin or the blank control solution. After 3 hr., methylated catechin started to crystallise, and work with this ceased.

A solution (50 ml.) of mollisacacidin trimethyl ether (20 mg.) in 50% aqueous ethanol had pH 5·8. The pH was adjusted to 10·6 with sodium carbonate solution. A solution (pH 10·8) of sodium borate (27 mg.) in 50% aqueous ethanol (100 ml.) was then added in portions. On addition of 0·6—1 ml. the pH fell to 8·5.

Oxidation with Potassium Permanganate.—Mollisacacidin trimethyl ether (1 g.), potassium permanganate (2·5 g.), and acetone (100 ml.) were heated under reflux for 4 hr., water was added, and the acetone evaporated under reduced pressure. The aqueous suspension was saturated with sulphur dioxide and extracted with ether. The acids were taken up with aqueous sodium hydrogen carbonate, recovered by acidification, and treated in dry ether for 2 hr. with excess of diazomethane in 1 : 1 ether–methanol. The methylated derivatives were recovered and triturated with 2N-sodium hydroxide solution.

An alkali-soluble ester A (m. p. 150—153°) was precipitated with hydrochloric acid and treated with potassium hydroxide (0·7 g.) in ethanol (10 ml.) and water (10 ml.) on a water-bath for 2 hr. The alcohol was removed and the solution diluted with water and extracted with ether. Evaporation of the ether afforded a white residue (150 mg.), which was dried ($CaCl_2$) and sublimed, giving fractions (i) (95 mg.), sublimes at 90—95°/0·2 mm., m. p. 144—148°, and (ii) (10 mg.), sublimes at 105—115°/0·2 mm., m. p. 164—168°. With 5% aqueous ferric chloride fraction (ii) gave no colour, whereas fraction (i) gave a wine-red colour. Further sublimation of fraction (i) at 70—72°/0·2 mm. afforded a colourless sublimate, m. p. 154—156° alone or mixed with synthetic 4-methoxysalicylic acid.

The alkali-insoluble ester B, after being kept for 24 hr. over silica gel, crystallised (250 mg.; m. p. 48—53°). It was hydrolysed with potassium hydroxide (1·2 g.) in water (20 ml.) and ethanol (15 ml.). After 3 hr., the free acid was recovered as previously and sublimed, giving three fractions. The last of these, when resublimed, had m. p. 182—184° unchanged and did not depress the m. p. of synthetic veratric acid.

Fustin from the Heartwood of Rhus glabra.—The finely ground air-dried heartwood (900 g.) was extracted twice with ethyl acetate (2 × 4 l.) under reflux for 4 hr. The combined solutions were filtered and evaporated at 60° under reduced pressure to a yellow residue (36 g.). Paper chromatography as above showed the presence of components of R_F 0·45 and 0·67, both staining blue.

The extract (5 g.) was treated with hot water (50 ml.) and filtered [insoluble material (X)]. The filtrate was chromatographed on a column of Solka-floc; elution with 6% aqueous acetic acid gave ten fractions (20 ml. each). Paper chromatography showed a clear separation of the component of R_F 0·45. The solutions (120 ml.) containing this were evaporated at 60° to 30 ml. and crystallised in 24 hr. Several recrystallisations from hot water gave fustin as colourless needles (0·9 g.), m. p. and mixed m. p. 213—215°, $\lambda_{max.}$ 235, 278, 310 mμ ($E^{1\%}_{1cm.}$ 657, 583, 268), $\lambda_{min.}$ 225, 250, 305 mμ ($E^{1\%}_{1cm.}$ 624, 180, 265) (Found, in a sample dried at 100°/0·2 mm.: C, 62·3; H, 4·1. Calc. for fustin $C_{15}H_{12}O_6$: C, 62·5; H, 4·2%). Methylated with diazomethane,

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as previously, fustin readily formed a trimethyl ether, needles, m. p. 141—142° (from methanol) (lit., 143—144°).

The yellow insoluble material (X) was dissolved in a minimum volume of boiling methanol and rapidly filtered. Cooling gave yellow needles of fisetin, m. p. 350°, $\lambda_{max.}$ 316, 365 mμ ($E^{1\%}_{1cm.}$ 421, 770), $\lambda_{min.}$ 280, 325 mμ ($E^{1\%}_{1cm.}$ 164, 383).

Catalytic Reduction of Fustin.—Fustin (1·4 g.) in absolute methanol (100 ml.) containing platinum oxide (0·1 g.) absorbed 130 ml. of hydrogen in 4 hr. The solution was filtered, evaporated, and analysed on Whatman's No. 2 filter paper with aqueous 6% acetic acid as developer. Fustin and mollisacacidin were chromatographed alongside the reduction product(s). The developed chromatogram showed unchanged fustin (R_F 0·45) and a product with the same R_F as mollisacacidin (0·64). Accordingly, the solvent was removed and the residue dissolved in ethyl acetate (100 ml.) and extracted with water. Evaporation of the aqueous phase yielded a colourless residue (0·6 g.), recrystallisation of which from hot water gave needles with an indefinite m. p. Above 130°, the compound rapidly reddens (Found, in a sample dried at 56°/0·2 mm.: C, 55·6; H, 5·3. Calc. for $C_{15}H_{14}O_6,2H_2O$: C, 55·2; H, 5·5%). Methylated with diazomethane, the compound formed a trimethyl ether, m. p. 129° (sinter 76—77°), alone or mixed with mollisacacidin trimethyl ether. The infrared spectra of the synthetic compound and mollisacacidin over the skeletal range 700—1700 cm.$^{-1}$ were identical.

Conversion of the leuco*Anthocyanidins into Fisetinidin Chloride.*—Mollisacacidin (0·3 g.) was refluxed with 2 ml. of a 5 : 1 mixture of propan-2-ol and 3N-hydrochloric acid for 1 hr., then evaporated at 80° under reduced pressure. A portion (83 mg.) of the red amorphous residue was applied in alcohol (1 ml.) to Whatman's No. 3 MM. filter paper. The paper was developed with acetic acid–water–concentrated hydrochloric acid (30 : 10 : 3). After 18 hr., the band of anthocyanidin was cut out and the anthocyanidin recovered by elution with methanol. Evaporation of the solvent gave the chromatographically pure product (6·8 mg.). The anthocyanidin was compared against the anthocyanidin produced from the synthetic *leuco*anthocyanidin, and against fisetinidin chloride and pelargonidin. All four showed a pink spot of R_F 0·67—0·69 with the above solvent mixture. Pelargonidin had $\lambda_{max.}$ 530 mμ unaffected by addition of 0·2% aluminium chloride solution, but the other three compounds changed colour from red to blue and showed $\lambda_{max.}$ shifts from 525 to 570 mμ on formation of the aluminium complex.

Isolation of Pinitol.—Fraction II, in aqueous ethanol, gave white rhombs, m. p. 185—186·5°, alone or mixed with pinitol.

Isolation of the "Steroid".—Fraction III was shaken in ether with 4% sodium hydroxide solution, then with water, dried (Na_2SO_4), and evaporated at room temperature. The gummy residue was triturated with light petroleum (b. p. 40—60°). A white amorphous insoluble residue (1·2 g.) crystallised from 95% methanol as needles, m. p. 158—160° (1·0 g.). These were dried and treated with acetic anhydride (10 ml.) in pyridine (15 ml.) on a boiling-water bath. After 30 min. excess of anhydride was destroyed and the *acetate* recovered. Recrystallised several times from methanol it formed colourless plates, m. p. 167—169° (Found, in a sample dried at 100°/0·2 mm.: C, 81·0; H, 11·3. $C_{28}H_{48}O_2$ requires C, 80·8; H, 11·5. $C_{29}H_{50}O_2$ requires C, 80·9; H, 11·7%). The acetate (0·3 g.) was hydrolysed for 30 min. with boiling 10% alcoholic potassium hydroxide, poured into water, and extracted with ether. Evaporation of the ether yielded the colourless *product*, which recrystallised from methanol in colourless needles, m. p. 160—161°, $\lambda_{max.}$ 260 mμ (log ε 2·97), $\lambda_{min.}$ 238 mμ (log ε 2·16) (Found, in a sample dried at 100°/0·2 mm.: C, 83·0; H, 12·0. $C_{26}H_{46}O$ requires C, 83·35; H, 12·4. $C_{27}H_{48}O$ requires C, 83·4; H, 12·45%).

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526. *Synthesis of Gentianine.*

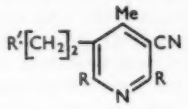
By T. R. Govindachari, K. Nagarajan, and S. Rajappa.

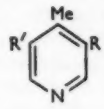
Treatment of 4-methyl-5-vinylnicotinic acid (IIa) with formaldehyde yields gentianine (III).

The alkaloid, gentianine, was recently [1] assigned structure (III) by degradation and by synthesis of its dihydro-derivative (IIIa). The synthesis of gentianine by an analogous method is reported in this paper.

The condensation product (I) [2,3] of α-aceto-γ-butyrolactone with cyanoacetamide was converted by phosphoryl chloride into 2 : 6-dichloro-5-2′-chloroethyl-3-cyano-4-methylpyridine (Ia) and thence into 5-2′-chloroethyl-4-methylnicotinonitrile (Ib) by hydrogenation over palladium. Attempts to prepare 4-methyl-5-vinylnicotinic acid (IIa) from the nitrile by alcoholic alkali, by dehydrochlorination,[2] and hydrolysis of the nitrile group [4] failed: the claim by McElvain and Goese [4] to have effected alkaline hydrolysis of 4-methylnicotinonitrile to 4-methylnicotinic acid could not be confirmed by Webb and Corwin.[5] Acid hydrolysis of the nitrile (Ib) yielded intractable products. With excess of

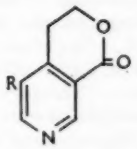
(I): R = R′ = OH.
(Ia): R = R′ = Cl.
(Ib): R = H, R′ = Cl.
(Ic): R = H, R′ = NEt_2.

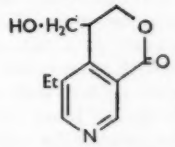




(II): R = CN, R′ = $CH{:}CH_2$.
(IIa): R = CO_2H, R′ = $CH{:}CH_2$.
(IIb): R = CO_2H, R′ = $[CH_2]_2{\cdot}NEt_2$.

(III): R = $CH{:}CH_2$.
(IIIa): R = Et.





(IV)

diethylamine the nitrile (Ib) yielded two products: the higher-boiling fraction gave analyses correct for the diethylamino-compound (Ic) which, however, could not be hydrolysed to the acid (IIb). Analyses of the lower-boiling product were correct for 4-methyl-5-vinylnicotinonitrile (II), and this structure was unambiguously proved by preparation from the nitrile (Ib) on treatment with trimethylamine, partly by direct dehydrochlorination and partly by Hofmann degradation of the quaternary compound. Acid hydrolysis of the nitrile (II) gave a satisfactory yield of 4-methyl-5-vinylnicotinic acid (IIa), its structure being confirmed by identity of its dihydro-derivative with the known 5-ethyl-4-methylnicotinic acid.[1]

Treatment of the sodium salt of the acid (IIa) with the calculated quantity of formaldehyde, under conditions employed for the synthesis of dihydrogentianine,[1] yielded only minute amounts of gentianine (isolated as the picrate). That the vinyl group has a deactivating effect on the adjacent 4-methyl group in the reaction with formaldehyde was confirmed by substantial recovery of gentianine after it had been heated with excess of formaldehyde under conditions which convert dihydrogentianine into the lactone (IV). Finally treatment of the sodium salt of the acid (IIa) with excess of formaldehyde gave a moderate yield of gentianine (III) identical with the natural substance.

Experimental

5-2′-Chloroethyl-4-methylnicotinonitrile.—3-Cyano-2 : 6-dihydroxy-5-2′-hydroxyethyl-4-methylpyridine [2,3] (4 g.) was heated with phosphorus oxychloride (10 ml.) at 200—210° for 4 hr., then poured on crushed ice. The solution was allowed to come to room temperature and

[1] Govindachari, Nagarajan, and Rajappa, *J.*, 1957, 551.
[2] Stevens, Beutel, and Chamberlin, *J. Amer. Chem. Soc.*, 1942, **64**, 1093.
[3] Ritchie, *Austral. J. Chem.*, 1956, **9**, 244.
[4] McElvain and Goese, *J. Amer. Chem. Soc.*, 1943, **65**, 2233.
[5] Webb and Corwin, *ibid.*, 1944, **66**, 1456.

extracted twice with ether. The combined extracts were washed with water and dried (Na_2SO_4) and the solvent was distilled off, yielding the crude trichloro-compound (3·7 g.). The combined product from 2 such batches was hydrogenated in methanol (50 ml.) containing potassium acetate (6 g.) and palladium chloride (0·45 g.) at 2 atm. till no more hydrogen was absorbed. The solution was filtered and the residue washed with methanol. The filtrate was evaporated and the residue treated with water (50 ml.), saturated with sodium hydrogen carbonate, and extracted repeatedly with ether. Evaporation of the dried (Na_2SO_4) ether extract and vacuum-distillation of the residual solid gave 5-2′-chloroethyl-4-methylnicotinonitrile (5·4 g.), b. p. 144—145°/3 mm., solidifying in the receiver, and yielding a *picrate* (from water), m. p. 143—144° (Found: C, 43·7; H, 3·0. $C_{15}H_{12}O_7N_5Cl$ requires C, 44·0; H, 2·9%).

4-Methyl-5-vinylnicotinonitrile.—(*a*) The preceding nitrile (4 g.) in alcohol (7 ml.) was heated with excess of diethylamine (8 ml.) in a bomb at 120° for 8 hr. The alcohol was then evaporated, and the residue diluted with water, basified with 2N-sodium hydroxide, and extracted repeatedly with ether. The dried (Na_2SO_4) ether extract on evaporation and fractionation under reduced pressure gave 4-methyl-5-vinylnicotinonitrile (1·8 g.), b. p. 98°/2 mm., yielding a *picrate*, m. p. 141—143° (from water) (Found, after drying at 30° for 24 hr.: C, 48·6; H, 2·7. $C_{15}H_{11}O_7N_5$ requires C, 48·3; H, 2·9%), and 5-2′-diethylaminoethyl-4-methylnicotinonitrile (1 g.), b. p. 134°/2 mm., yielding a *monopicrate* (prepared in aqueous acid), m. p. 172—173° (from alcohol) (Found: C, 51·2; H, 4·6. $C_{13}H_{19}N_3,C_6H_3O_7N_3$ requires C, 51·1; H, 4·9%), and a *dipicrate* (prepared in alcohol), m. p. 126—127° (from acetic acid–alcohol) (Found: C, 44·7; H, 3·6; N, 18·8. $C_{13}H_{19}N_3,2C_6H_3O_7N_3$ requires C, 44·4; H, 3·7; N, 18·7%).

(*b*) 5-2′-Chloroethyl-4-methylnicotinonitrile (1 g.) was heated in a bomb with trimethylamine (25% solution in methanol; 5 ml.) at 130° for 7 hr. The solvent was evaporated and the residue digested with dry ether. Evaporation of the extract and distillation of the residue (0·5 g.) gave an oil, b. p. 98°/2 mm., yielding a picrate, m. p. and mixed m. p. with 4-methyl-5-vinylnicotinonitrile picrate, m. p. 141—143°. The ether-insoluble residue was dissolved in water (100 ml.) and shaken with silver oxide (from 5 g. of silver nitrate) for 3 hr. The mixture was filtered and the residue washed with water. The total filtrates (200 ml.) were concentrated in a vacuum. When the last 10 ml. of the solution were evaporating, a solid (100 mg.) distilled with the steam. The picrate after crystallisation from water was identical with the picrate of 4-methyl-5-vinylnicotinonitrile.

4-Methyl-5-vinylnicotinic Acid.—4-Methyl-5-vinylnicotinonitrile (2 g.) was heated with 70% sulphuric acid (20 ml.) at 125—130° for 4 hr. The mixture was poured on crushed ice, and the solution treated with calcium hydroxide to pH 5—6 and filtered. The residue was repeatedly washed with boiling water. The combined filtrates were evaporated to dryness, extracted thoroughly with boiling alcohol, and filtered. The filtrate was evaporated to dryness and the residual amino-acid sulphate passed in aqueous solution through De-acidite-E (Permutit). Evaporation of the eluate and recrystallisation of the residue from alcohol–ether gave *4-methyl-5-vinylnicotinic acid* (0·8 g.), m. p. 178—180° (decomp.) (Found after drying at 70°: C, 60·0; H, 6·0. $C_9H_9O_2N,H_2O$ requires C, 59·7; H, 6·1%).

The above acid (50 mg.) in methanol (10 ml.) was hydrogenated at 50 lb. per sq. in. for 3 hr. after the addition of Adams catalyst (20 mg.). Filtration, evaporation, and crystallisation of the residue from alcohol gave 5-ethyl-4-methylnicotinic acid [1] (10 mg.), m. p. and mixed m. p. 163—165°.

Synthesis of Gentianine.—4-Methyl-5-vinylnicotinic acid (0·5 g.) in water (5 ml.) was treated with sodium hydrogen carbonate (0·3 g.) and 40% aqueous formaldehyde (5 ml.) and heated in a sealed tube at 100° for 10 hr. Excess of formaldehyde was then removed in steam. The solution was acidified, basified with solid sodium hydrogen carbonate after 1 hr., and extracted with chloroform. The dried (Na_2SO_4) extract was evaporated. Crystallisation of the residue (50 mg.) from light petroleum (b. p. 40—60°) gave *gentianine*, m. p. and mixed m. p. 80—81° (Found: C, 68·8; H, 4·9. $C_{10}H_9O_2N$ requires C, 68·6; H, 5·1%).

Gentianine (0·2 g.) in water (2 ml.) was heated with sodium hydrogen carbonate (0·2 g.) and 40% aqueous formaldehyde (3 ml.) at 100° for 15 hr. Working up as before resulted in the recovery of gentianine (0·1 g.), m. p. and mixed m. p. 80—81°.

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PRESIDENCY COLLEGE, MADRAS, INDIA. [*Received, January 28th,* 1957.]

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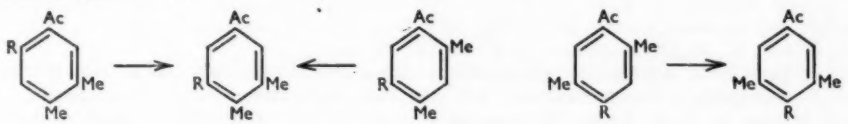
527. *The Isomerisation of Aromatic Ketones.*

By G. Baddeley and S. Varma.

The isomerisation of 4-alkyl-2 : 5-dimethylacetophenone by fusion with excess of aluminium chloride affords the 3 : 5-dimethyl isomer in useful yield only when the 4-alkyl group is methyl, ethyl, or perhaps propyl. Other 4-alkyl groups are replaced by either a hydrogen atom or a methyl group.

The acetophenone homologues (I), (II), and (III), where R is an alkyl group, are readily accessible from *o*-, *m*-, and *p*-xylene respectively and, from previously published work,[1] might be expected to provide the otherwise not readily accessible ketones (IV) and (V) by rearrangement through the agency of hydrogen chloride–aluminium chloride. 1 : 3 : 5-Trialkylbenzenes are readily obtained by Friedel–Crafts alkylation and rearrangement of benzene homologues, and isomerisation of their acetyl derivatives may provide another route to the 3 : 4 : 5-trialkylacetophenones. It is already known [1] that 2 : 4 : 6-trimethylacetophenone gives the 3 : 4 : 5-isomer in 80% yield and that this isomer is the main product of attempts to isomerise 4-*tert.*-butyl-2 : 6-dimethylacetophenone; *i.e.*, that the *tert.*-butyl group is replaced by methyl group.[2] We have found other examples of this peculiar replacement. The isomerisation of 2 : 4 : 5-trialkylacetophenone is the more difficult step in the preparation of 3 : 4 : 5- from 2 : 4 : 6-trialkyl derivatives and thereby determines the feasibility of the preparation. This paper is concerned with the rearrangement of 2 : 4 : 5-trialkyl derivatives and especially that of 4-alkyl-2 : 5-dimethylacetophenone (III ⟶ V).



(I) (IV) (II) (III) (V)

The rearrangement is now shown to have very limited application: it provides compound (V) in better than 70% yield only when R is H, Me, or Et; the yield is 39% when R is Pr, and the compound is not obtained when R is Pr^i, Bu^i, or CH_2Bu^t. Replacement of R by H accounts for 35 and 77% of the product when R is Pr and Pr^i, respectively, while replacement by Me provides 36 and 26% of the product when R is Bu^i and CH_2Bu^t, respectively.

The rearrangement (I ⟶ IV; R ≠ Me) requires a lower temperature and is more convenient than reaction (II ⟶ IV). Thus (IV; R = Pr) is obtained from (I) and (II; R = Pr) in yields of 49 and 31%, respectively. The propyl compound (II; R = Pr) also gave 2 : 4 : 5-trimethylacetophenone (10%).

Experimental

Materials.—4-Ethyl-2 : 5-dimethylacetophenone was prepared as described by Freund and Fleischer.[3]

2 : 5-*Dimethyl*-4-iso*propylacetophenone.*—The product of interaction of 2 : 5-dimethylacetophenone and methylmagnesium iodide gave 1 : 4-dimethyl-2-*iso*propenylbenzene, b. p. 190°/760 mm., by dehydration with formic acid (98%). Catalytic hydrogenation gave 1 : 4-*dimethyl*-2-iso*propylbenzene*, b. p. 190°/760 mm., n_D^{18} 1·5062 (Found: C, 89·4; H, 10·7. $C_{11}H_{16}$ requires C, 89·2; H, 10·8%). The required *ketone*, b. p. 151°/21 mm., n_D^{18} 1·5335, was obtained

[1] Baddeley, *J.*, 1944, 232; 1950, 994; Baddeley and Pendleton, *J.*, 1952, 807; Baddeley, Holt, and Pickles, *J.*, 1952, 4162; Baddeley and Williamson, *J.*, 1953, 2120.
[2] Pearson and Bruton, *J. Org. Chem.*, 1954, **19**, 957.
[3] Freund and Fleischer, *Annalen*, 1918, **414**, 38.

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by Friedel–Crafts acetylation in methylene chloride below 10°. Its *semicarbazone* separated from benzene in plates, m. p. 186° (Found: C, 67·7; H, 8·2; N, 17·2. $C_{14}H_{21}ON_3$ requires C, 68·0; H, 8·5; N, 17·0%), and its 2 : 4-*dinitrophenylhydrazone* from acetic acid in orange needles, m. p. 217° (Found: C, 61·6; H, 5·7; N, 15·6. $C_{19}H_{22}O_4N_4$ requires C, 61·6; H, 5·9; N, 15·1%). Oxidation of the ketone with dilute nitric acid gave benzene-1 : 2 : 4 : 5-tetracarboxylic acid (tetramethyl ester, m. p. and mixed m. p. 141°).

2 : 5-*Dimethyl*-4-n-*propylacetophenone*.—Clemmensen reduction of 2 : 5-dimethylpropiophenone [4] [*semicarbazone*, m. p. 169° (Found: C, 65·6; H, 7·6. $C_{12}H_{17}ON_3$ requires C, 65·8; H, 7·8%)] gave 1 : 4-dimethyl-2-*n*-propylbenzene,[5] n_D^{22} 1·5045, from which the required *ketone*, b. p. 146—147°/17 mm., n_D^{23} 1·5272, was obtained by acetylation. The *semicarbazone* separated from aqueous ethanol in rods, m. p. 160° (Found: C, 68·0; H, 8·7; N, 17·1. $C_{14}H_{21}ON_3$ requires C, 68·0; H, 8·5; N, 17·0%), and the 2 : 4-*dinitrophenylhydrazone* from acetic acid in orange flakes, m. p. 151·5° (Found: C, 61·8; H, 6·0; N, 15·4. $C_{19}H_{22}O_4N_4$ requires C, 61·6; H, 5·9; N, 15·1%). Tetramethyl benzene-1 : 2 : 4 : 5-tetracarboxylate was obtained from the ketone by oxidation and esterification.

4-*iso*Butyl-2 : 5-dimethylacetophenone was similarly prepared and identified. 2-iso*Butyl*-1 : 4-*dimethylbenzene*, b. p. 86°/14 mm., n_D^{19} 1·4981 (Found: C, 89·0; H, 10·7. $C_{12}H_{18}$ requires C, 88·9; H, 11·1%), gave the required ketone, b. p. 150°/17 mm.; *semicarbazone*, m. p. 184° (Found: N, 16·2. $C_{15}H_{23}ON_3$ requires N, 16·1%), and 2 : 4-*dinitrophenylhydrazone*, m. p. 134—135° (Found: C, 62·7; H, 5·9; N, 15·2. $C_{20}H_{24}O_4N_4$ requires C, 62·5; H, 6·3; N, 14·6%).

2 : 5-*Dimethyl*-4-neo*pentylacetophenone*, b. p. 157°/17 mm., n_D^{22} 1·5230, was prepared from 1 : 4-dimethyl-2-*neo*pentylbenzene, b. p. 106°/22 mm., n_D^{22} 1·4985. The hydrocarbon was obtained in 50% yield by interaction under reflux for 3 hr. of the Grignard derivative of 2 : 5-dimethylbenzyl chloride [6] and a molecular proportion of *tert.*-butyl bromide; dry benzene was then added and the mixture was refluxed for a further 30 hr. The ketone gave a *semicarbazone*, m. p. 213° (Found: N, 15·4. $C_{16}H_{25}ON_3$ requires N, 15·3%), a 2 : 4-*dinitrophenylhydrazone*, m. p. 166° (Found: C, 62·8; H, 6·6; N, 13·9. $C_{21}H_{26}O_4N_4$ requires C, 63·3; H, 6·5; N, 14·1%), and an *oxime*, needles, m. p. 134—135°, from aqueous methanol (Found: C, 76·7; H, 9·6; N, 5·9. $C_{15}H_{23}ON$ requires C, 77·3; H, 9·9; N, 6·0%).

4 : 5-Dimethyl-2-*n*-propylacetophenone, b. p. 150—151°/25 mm., $n_D^{21\cdot5}$ 1·5245, was prepared from 1 : 2-dimethyl-4-*n*-propylbenzene,[7] and gave a *semicarbazone*, m. p. 131—132° (Found: C, 67·6; H, 8·6; N, 16·6. $C_{14}H_{21}ON_3$ requires C, 68·0; H, 8·5; N, 17·0%), and a 2 : 4-*dinitrophenylhydrazone*, m. p. 94° (Found: C, 61·7; H, 6·1; N, 15·0. $C_{19}H_{22}O_4N_4$ requires C, 61·6; H, 5·9; N, 15·1%).

2 : 4-Dimethyl-5-propylacetophenone, b. p. 142—144°/16 mm., n_D^{22} 1·5239 [*semicarbazone*, m. p. 144—145° (Found: C, 67·9; H, 8·6; N, 17·3. $C_{14}H_{21}ON_3$ requires C, 68·0; H, 8·5; N, 17·0%), and 2 : 4-*dinitrophenylhydrazone*, m. p. 173° (Found: C, 61·5; H, 5·8; N, 15·1. $C_{19}H_{22}O_4N_4$ requires C, 61·6; N, 5·9; N, 15·1%)], was prepared from 1 : 3-dimethyl-4-*n*-propylbenzene.[8]

The Isomerisation of the Ketones.—A mixture of the ketone, aluminium chloride (2·7 mol.) and sodium chloride (0·6 mol.) was heated for 4 hr. at a selected temperature and subsequently worked up in the usual manner.

2 : 4 : 5-Trimethylacetophenone [semicarbazone, m. p. 204° (Found: N, 19·3. Calc. for $C_{13}H_{17}ON_3$: N, 19·2%)] on reaction at 140° gave 3 : 4 : 5-trimethylacetophenone [1] (79%), b. p. 140—142°/18 mm. (semicarbazone, m. p. and mixed m. p. 217°).

4-Ethyl-2 : 5-dimethylacetophenone on reaction at 125° gave 4-ethyl-3 : 5-dimethylacetophenone (73%), b. p. 153—156°/22 mm., n_D^{18} 1·5410 [*semicarbazone*, m. p. 189—190° (Found: N, 18·3. $C_{13}H_{19}ON_3$ requires N, 18·0%)]. Oxidation of the product with dilute nitric acid gave benzene-1 : 2 : 3 : 5-tetracarboxylic acid (tetramethyl ester, m. p. and mixed m. p. 111°).

2 : 5-Dimethyl-4-propylacetophenone on reaction at 125° gave (*a*) 3 : 5-dimethylacetophenone (35%), which was identified by its semicarbazone and by oxidation to benzene-1 : 3 : 5-tricarboxylic acid, and (*b*) 3 : 5-dimethyl-4-propylacetophenone (39%), b. p. 107—109°/0·5 mm. [*semicarbazone*, m. p. 208—209° (Found: C, 68·0; H, 8·6; N, 17·3. $C_{14}H_{21}ON_3$ requires C,

[4] Claus and Fickert, *Ber.*, 1886, **19**, 3183.
[5] Uhlhorn, *Ber.*, 1890, **23**, 2350.
[6] Braun and Nelles, *Ber.*, 1934, **67**, 1096.
[7] Auwers and Ziegler, *Annalen*, 1921, **425**, 260.
[8] Nightingale and Carton, *J. Amer. Chem. Soc.*, 1940, **62**, 280.

68·0; H, 8·5; N, 17·0%)]. It gave benzene-1 : 2 : 3 : 5-tetracarboxylic acid when oxidised with dilute nitric acid.

4-*iso*Butyl-2 : 5-dimethylacetophenone on reaction at 125° gave (*a*) 2 : 4 : 5-trimethylacetophenone (36%), which was identified by its semicarbazone, m. p. and mixed m. p. 204°, its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 246°, and by oxidation to benzene-1 : 2 : 4 : 5-tetracarboxylic acid; and (*b*) initial ketone (30%) which was similarly identified. It is remarkable that the 2-methyl group has not migrated to the 3-position.

2 : 5-Dimethyl-4-*neo*pentylacetophenone behaved similarly, affording 2 : 4 : 5-trimethylacetophenone (26%) and initial ketone (42%).

2 : 5-Dimethyl-4-*iso*propylacetophenone on reaction at 100° gave 2 : 5-dimethylacetophenone (77%), which was identified by its semicarbazone and by hypochlorite oxidation to 2 : 5-dimethylbenzoic acid, m. p. and mixed m. p. 132°.

4 : 5-Dimethyl-2-propylacetophenone on reaction at 100° gave 3 : 4-dimethylacetophenone (22%) and 3 : 4-dimethyl-5-propylacetophenone (49%), b. p. 155—158°/17 mm. [*semicarbazone*, m. p. 155—155·5° (Found : C, 68·3; H, 8·2; N, 17·1. $C_{14}H_{21}ON_3$ requires C, 68·0; H, 8·5; N, 17·0%), and 2 : 4-*dinitrophenylhydrazone*, m. p. 171—172° (Found : C, 61·8; H, 5·8; N, 15·2. $C_{19}H_{22}O_4N_4$ requires C, 61·6; H, 5·9; N, 15·1%)]; it gave benzene-1 : 2 : 3 : 5-tetracarboxylic acid when oxidised with dilute nitric acid.

2 : 4-Dimethyl-5-propylacetophenone on reaction at 125° gave 2 : 4 : 5-trimethylacetophenone (10%), initial ketone (10%), and 3 : 4-dimethyl-5-propylacetophenone (31%).

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY. [*Received, February 6th*, 1957.]

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528. *The Indirect Synthesis of* 2 : 2′-*Dihydroxy*-3 : 3′-*di*-(2-*hydroxybenzyl*)*diphenylmethane*.

By P. A. JENKINS.

2 : 2′-Dihydroxy-3 : 3′-di-(2-hydroxybenzyl)diphenylmethane has been synthesised by condensation of 3 : 5 : 5′-trichloro-2 : 2′-dihydroxydiphenylmethane with formaldehyde, followed by dehalogenation. Modification of the initial condensation caused cyclic acetal formation, subsequent reduction of the intermediate giving 8-2′-hydroxybenzylbenzo-1 : 3-dioxan.

A STUDY [1] of the phenol–formaldehyde condensation in the preparation of " high ortho " Novolak resins required the synthesis of a number of possible intermediates as standards for comparison by paper chromatography and infrared spectroscopy. One of these was the previously unreported 2 : 2′-dihydroxy-3 : 3′-di-(2-hydroxybenzyl)diphenylmethane (I). A number of workers [2, 3, 4] have employed halogen-blocking of some of the reactive positions of the phenolic nucleus, in order to obtain compounds with the required substitution, the halogen being later removed. The starting material, in this case, 3 : 5 : 5′-trichloro-2 : 2′-dihydroxydiphenylmethane (II), was prepared by condensing 2 : 4-dichloro-6-hydroxymethylphenol [5] with an excess of *p*-chlorophenol under acid conditions.[6]

This compound with aqueous formaldehyde in the presence of acetic and sulphuric acid appeared to require the presence of hydrochloric acid to give good yields of 5 : 5′-dichloro-3 : 3′-di-(3 : 5-dichloro-2-hydroxybenzyl)-2 : 2′-dihydroxydiphenylmethane (III), consistently with the chloromethylation of the dihydroxydiphenylmethane described by Finn, James, and Standen.[4] In the absence of hydrochloric acid, an appreciable quantity of the cyclic acetal (IV) was also formed and if the half-molar proportion of formaldehyde was replaced by a molar quantity of trioxymethylene it formed the bulk of the product.

[1] Fraser, Hall, Jenkins, and Raum, unpublished works.
[2] Bender, Farnham, Guyer, Apel, and Gibb, *Ind. Eng. Chem.*, 1952, **44**, 1619.
[3] Carpenter and Hunter, *J. Appl. Chem.*, 1951, **1**, 217; Davis, Hayes, and Hunter, *ibid.*, 1953, **3**, 312; Carpenter and Hunter, *ibid.*, p. 486.
[4] Finn, James, and Standen, *ibid.*, 1954, **4**, 296, 497.
[5] G.P. 510,447.
[6] F. Addn. P. 39,585/1930; *Chem. Abs.*, 1932, **26**, 4827.

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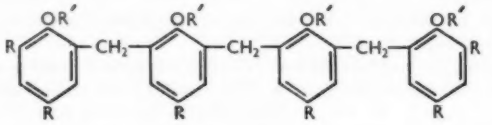
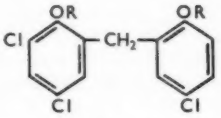
Indeed, the cyclic acetal group was formed so readily that use of the acetyl or ethoxycarbonyl derivatives (V and VI) was considered : this, however, was abandoned when the diacetyl derivative had been recovered substantially unchanged after several hours' refluxing with formaldehyde in the presence of acetic and sulphuric acid.

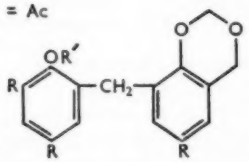
The final stage in the synthesis, the removal of chlorine from the hexachloro-derivative to give the required tetranuclear " Novolak," was easily accomplished by using Raney alloy in the presence of sodium hydroxide, the method also being successful in the reduction of the chlorinated benzylbenzodioxan.



(I) R = R′ = H
(III) R = Cl, R′ = H
(VII) R = H, R = Ac



(II) R = H
(V) R = Ac
(VI) R = CO_2Et



(IV) R = Cl, R′ = H
(VIII) R = R′ = H
(IX) R = H, R′ = Ac

The structures of the two compounds are supported by the infrared spectra, that of the four-ring compound being similar to that of 2 : 6-di-(2-hydroxybenzyl)phenol prepared by condensing 4-bromo-2 : 6-di(hydroxymethyl)phenol with an excess of *p*-bromophenol under acid conditions, followed by dehalogenation.[2] That the central methylene bridge joining the nuclei did not involve the phenolic hydroxyl groups was shown by the absence of absorption due to an ether linkage. The spectrum of 8-2′-hydroxybenzyl-1 : 3-benzodioxan did however show the presence of a cyclic ether linkage.

Experimental

2 : 4-Dichloro-6-hydroxymethylphenol was prepared in variable yield (26—38%) by the hydroxymethylation of 2 : 4-dichlorophenol in alkaline solution at 45° for 20 hr.

3 : 5 : 5′-*Trichloro*-2 : 2′-*dihydroxydiphenylmethane* (II).—2 : 4-Dichloro-6-hydroxymethylphenol (20 g.), *p*-chlorophenol (63 g.), and concentrated hydrochloric acid (1·5 ml.) were stirred at 60—70° for approx. 17 hr. After a further 1 hr. at 100° (bath) the mixture was cooled to room temperature and the solid removed on a sintered-glass filter. The residual solid (24 g.) had m. p. 184—185° after it had been washed with carbon tetrachloride, raised to 185—186° (lit.,[6] m. p. 187°) on recrystallisation from benzene (Found : C, 51·2; H, 3·0; Cl, 34·8. Calc. for $C_{13}H_8O_2Cl_3$: C, 51·4; H, 3·0; Cl, 35·1%).

The 2 : 2′-*diacetoxy-derivative* (V) was prepared by refluxing with acetic anhydride. After recrystallisation from methanol and then light petroleum (b. p. 60—80°), it had m. p. 107—108° (Found : C, 53·2; H, 3·6; Cl, 27·3. $C_{17}H_{13}O_4Cl_3$ requires C, 52·6; H, 3·35; Cl, 27·5%).

3 : 5 : 5′-*Trichloro*-2 : 2′-*di*(*ethoxycarbonyloxy*)*diphenylmethane* (VI).—Redistilled ethyl chloroformate (11·4 ml.) in chloroform (30 ml.) was cooled to *ca.* −20° and 3 : 5 : 5′-trichloro-2 : 2′-dihydroxydiphenylmethane (9·1 g.) in pyridine (10 ml.) and chloroform (30 ml.) was added fairly rapidly to give a yellow solution. The cooling bath was then removed, and after a further quantity of pyridine (5 ml.) had been added, the temperature of the solution was allowed to reach that of the room, a red colour gradually developing. Next morning the solution was refluxed for an hour, then cooled, and the chloroform washed several times with water to remove pyridine hydrochloride. The chloroform solution was dried (Na_2SO_4) and evaporated to an oil (12·8 g.) which with light petroleum (b. p. 40—60°) gave the *ester* (12·2 g.), m. p. 92·5°.

Recrystallisation from methanol raised the m. p. to 95—97°, unchanged on further recrystallisation from light petroleum (b. p. 100—120°) (Found : C, 51·3; H, 3·8; Cl, 23·5. $C_{19}H_{17}O_6Cl_3$ requires C, 50·9; H, 3·8; Cl, 23·8%).

5 : 5′-*Dichloro*-3 : 3′-*di*-(3 : 5-*dichloro*-2-*hydroxybenzyl*)-2 : 2′-*dihydroxydiphenylmethane* (III). —3 : 5 : 5′-Trichloro-2 : 2′-dihydroxydiphenylmethane (6·1 g.), acetic acid (15 ml.), concentrated hydrochloric acid (3 ml.) 40% aqueous formaldehyde (0·91 ml., 0·55 mol.), and concentrated sulphuric acid (0·3 ml.), were heated under reflux for 4 hr., an appreciable quantity of pink material separating. After cooling to room temperature, this solid (4·5 g.), m. p. 222° (decomp.), was filtered off, washed with a mixture of acetic acid (5 vol.) and water (1 vol.), and dried. The filtrate and washings were combined and refluxed for a further 5 hr., further solid (0·9 g.), m. p. 210° (decomp.), separating on cooling. Addition of water to the mother-liquor from this second crop produced some unchanged starting material. Recrystallisation from toluene (charcoal) gave the required 5 : 5′-*dichloro*-3 : 3′-*di*-(3 : 5-*dichloro*-2-*hydroxybenzyl*)-2 : 2′-*dihydroxydiphenylmethane*, m. p. 230° (decomp.) [Found : C, 51·9; H, 3·2; Cl, 34·0%; *M* (in acetone), 639, 620. $C_{27}H_{18}O_4Cl_6$ requires C, 52·3; H, 2·9; Cl, 34·4%; *M*, 619].

2 : 2′-*Dihydroxy*-3 : 3′-*di*-(2-*hydroxybenzyl*)*diphenylmethane* (I).—The above hexachloro-compound (4 g.) in 5% aqueous sodium hydroxide (82 ml.) was stirred on a steam-bath and 50/50 Raney alloy (13 g.) added portionwise. After a further 2 hours' heating, nickel was filtered off and the solution poured into concentrated hydrochloric acid. Solid which separated was filtered off, boiled with acidulated water, and dried. Crystallisation from carbon tetrachloride (charcoal) gave the *product* (2·2 g.), m. p. 152—154°, raised to 159—160° on further recrystallisation from benzene. After drying for 2 hr. at 100° over phosphoric oxide at 0·1 mm. the m. p. was 161—162° (Found : C, 79·0; H, 6·15; Cl, 0. $C_{27}H_{24}O_4$ requires C, 78·6; H, 5·8%).

2 : 2′-*Diacetoxy*-3 : 3′-*di*-(2-*acetoxybenzyl*)*diphenylmethane* (VII).—The above halogen-free compound (1 g.) was refluxed with acetic anhydride (15 ml.) and concentrated sulphuric acid (2 drops) for 3 hr. Acetic anhydride was then removed under reduced pressure and the residue treated with aqueous methanol, then methanol. The insoluble material (1·03 g.), m. p. 110—112°, was recrystallised from ethanol (charcoal) and again from methanol to give a final m. p. of 126°. For analysis the *product* was dried over phosphoric oxide at 50°/0·15 mm. for 1 hr. (Found : C, 72·1; H, 5·6. $C_{35}H_{32}O_8$ requires C, 72·4; H, 5·5%).

6-*Chloro*-8-(3 : 5-*dichloro*-2-*hydroxybenzyl*)*benzo*-1 : 3-*dioxan* (IV).—3 : 5 : 5′-Trichloro-2 : 2′-dihydroxydiphenylmethane (10·2 g.) in glacial acetic acid (40 ml.) was stirred with trioxymethylene (2 g.) at 35—40°, and concentrated sulphuric acid (0·5 ml.) added. The temperature was raised to 50—55° for 1 hr., then to 90° for 2 hr. After cooling to room temperature, the crystalline magma was filtered and the solid (9·1 g.; m. p. 135°) washed with glacial acetic acid, then water. Recrystallisation from 1 : 1 benzene–light petroleum (b. p. 60—80°) yielded the *product* (5·5 g.), m. p. 141—147°, which after two recrystallisations from trichloroethylene had an unchanging m. p. 147—148° (Found : C, 52·5; H, 3·4; Cl, 30·5. $C_{15}H_{11}O_3Cl_3$ requires C, 52·1; H, 3·2; Cl, 30·8%).

8-2′-*Hydroxybenzylbenzo*-1 : 3-*dioxan* (VIII).—6-Chloro-8-(3 : 5-dichloro-2-hydroxybenzyl)-benzo-1 : 3-dioxan (4·1 g.) was treated with 10% aqueous sodium hydroxide (80 ml.) and water (160 ml.), a trace remaining undissolved. Raney alloy (8 g.) was added portionwise during an hour, with slight warming, and, after the mixture had been stirred overnight, the nickel was filtered off. The filtrate and washings were acidified with fairly concentrated hydrochloric acid, and the resulting precipitate (2·3 g.), m. p. 85—87°, was filtered off and washed with acid, then water. Recrystallisation of this chlorine-free material from 2 : 1 light petroleum (b. p. 60—80°)–trichloroethylene (charcoal) yielded the *product* (1·38 g.), m. p. 89—90° unchanged by further recrystallisation from 1 : 1 benzene–light petroleum (b. p. 60—80°) [Found : C, 74·3; H, 6·0%; *M* (in phenol), 236, 238. $C_{15}H_{14}O_3$ requires C, 74·8; H, 5·8%; *M*, 242].

The *acetoxy-derivative* (IX), after recrystallisation in turn from ethanol and methanol, had m. p. 60—62° (Found : C, 71·6; H, 5·6. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·6%).

Thanks are offered to Mr. D. G. Butt for experimental assistance, and to Mr. A. R. Philpotts for examination of the infrared spectra.

THE DISTILLERS COMPANY LIMITED, RESEARCH & DEVELOPMENT DEPARTMENT,
GREAT BURGH, EPSOM. [*Received, February 8th*, 1957.]

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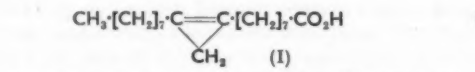
529. *Sterculic Acid. The Synthesis of Some Related β-Diketones and cyclo*Propanes.

By D. G. Brooke and J. C. Smith.

β-Diketones have been prepared, including 9 : 11-dioxononadecanoic acid, which has been shown to be identical with the ozonolysis product of sterculic acid. From the diketones, *via* the glycols and the dibromides, *cyclo*propanes have been made for comparison with dihydrosterculic acid.

The dioxo-acid obtained by catalytic reduction of the ozonide of sterculic acid (I) was shown [1,2] to be 9 : 11-dioxononadecanoic acid (II; $x = 7$, R = H). By Adams and Hauser's method [3] the β-diketones (II), (III), and (IV) have been prepared. In the presence of sodium amide and twice the theoretical amount of ethyl heptanoate, methyl undecyl ketone yielded 7 : 9-dioxoeicosane (IV; $m = 5$, $n = 10$). Ethyl nonanoate and methyl undecyl ketone similarly yielded 9 : 11-dioxodocosane (IV; $m = 7$, $n = 10$); ethyl heptanoate and hexyl methyl ketone gave 7 : 9-dioxopentadecane (IV; $m = n = 5$). The three diketones were isolated as their copper derivatives.

From equimolecular proportions of dimethyl azelaate and methyl octyl ketone the main product appeared to be 9 : 11 : 19 : 21-tetraoxononacosane (III; $x = 7$) with only a trace of the ester (II; $x = 7$, R = CH_3). When, however, two molecular proportions of dimethyl azelaate were employed the product was almost entirely methyl 9 : 11-dioxononadecanoate (II; $x = 7$, R = CH_3). Similarly hexyl methyl ketone gave 7 : 9 : 17 : 19-tetraoxopentacosane (III; $x = 5$) and methyl 9 : 11-dioxoheptadecanoate (II; $x = 5$, R = CH_3).



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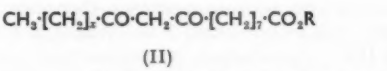

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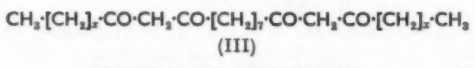

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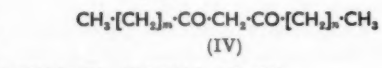

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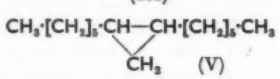

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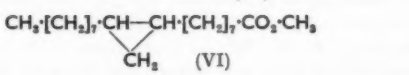

(VI)

The corresponding dioxononadecanoic acid (II; $x = 7$, R = H) was identical in m. p., mixed m. p., and infrared spectrum with the product obtained from sterculic acid by Faure and Smith.[2] 9 : 11-Dioxoheptadecanoic acid (II; $x = 5$, R = H) was obtained similarly. All these compounds, as β-diketones, gave intense red colours with alcoholic ferric chloride, and readily formed copper derivatives. That the Adams and Hauser condensation had, in these cases also, occurred at the methyl rather than at the methylene group of the ketones was shown by (i) the failure of the products to yield sodium hydrogen sulphite addition compounds and give the iodoform reaction, (ii) their ability to form urea complexes in high yield, and (iii) their alkaline hydrolysis to the expected products.

On reduction with potassium borohydride 7 : 9-dioxopentadecane gave pentadecane-7 : 9-diol. The corresponding dibromide gave, on treatment with sodium iodide and zinc in acetone,[4] a bromine-free product with the expected properties of 1 : 2-dihexyl*cyclo*propane (V). Similarly, but by the use of sodium borohydride, methyl 9 : 11-dioxoheptadecanoate and methyl 9 : 11-dioxononadecanoate were converted into *cyclo*propanes.

All these *cyclo*propane derivatives show infrared absorption at 3·27—3·30 μ and 9·83 μ.

[1] Nunn, *J.*, 1952, 313.
[2] Faure and Smith, *J.*, 1956, 1818.
[3] Adams and Hauser, *J. Amer. Chem. Soc.*, 1944, **66**, 1220.
[4] Hall, Lewis, and Polgar, *J.*, 1955, 3971; Hass, McBee, Hinds, and Gluesenkamp, *Ind. Eng. Chem.*, 1936, **28**, 1178; Shortridge, Craig, Greenlee, Derfer, and Boord, *J. Amer. Chem. Soc.*, 1948, **70**, 946.

Cole [5] attributes the absorption at 3040—3058 cm.$^{-1}$ (3·27—3·30 μ) to methylene in a *cyclo*propane ring, and states that the band at 1010 cm.$^{-1}$ (9·83 μ) is unreliable when oxygen functions are present. The medium band at 9·83 μ in 1 : 2-dihexyl*cyclo*propane strengthens the case for attributing the 9·8 μ band in the spectrum of dihydrosterculic acid itself to the presence of a *cyclo*propane ring.

Experimental

7 : 9-*Dioxoeicosane.*—Clean sodium (15·2 g.) was added in small portions with stirring to anhydrous liquid ammonia (300 c.c.), together with a small crystal of ferric nitrate to catalyse the conversion of the sodium into amide. When this conversion was complete ammonia was evaporated (steam-bath), sufficient anhydrous ether being added to keep the volume of liquid at approximately 300 c.c. After nearly all the ammonia had evaporated (indicated by the refluxing of the ether) the suspension of sodium amide was stirred and refluxed for a few minutes, then cooled to room temperature.

Methyl undecyl ketone (59·4 g., 0·3 mole; m. p. 29°) in dry ether (50 c.c.) was added to the stirred suspension of sodium amide during 5—10 min. After a further 5 min. ethyl heptanoate (94·8 g., 0·6 mole; b. p. 187°) in dry ether (50 c.c.) was added, and the stirring and refluxing continued for 2 hr. The mixture was poured into water (300 c.c.), neutralised with dilute hydrochloric acid, and extracted with ether, yielding a viscous liquid which was dissolved in an equal volume of methanol. A hot filtered solution of copper acetate (40 g.) in water (350 c.c.) was added to the methanol solution and the mixture allowed to cool to room temperature. The air-dried product was washed with light petroleum (b. p. 40—60°; 100 c.c.), and again dried. A small sample, recrystallised from methanol, gave the *copper salt* of 7 : 9-dioxoeicosane as pale blue crystals, m. p. 88° (Found: C, 70·5; H, 11·0. $C_{40}H_{76}O_4Cu$ requires C, 70·4; H, 10·9%).

The impure salt was shaken with sulphuric acid (10%; 500 c.c.) and ether (200 c.c.) until the ethereal layer was pale yellow. The aqueous acid layer was again extracted with ether and the combined ethereal solutions dried (Na_2SO_4). The solvent was distilled and the residue, fractionated *in vacuo* through a 20-cm. Vigreux column, yielded 7 : 9-*dioxoeicosane* (12 g.), b. p. 210°/12 mm., m. p. 27° (Found: C, 77·4; H, 12·2. $C_{20}H_{38}O_2$ requires C, 77·4; H, 12·2%).

9 : 11-*Dioxodocosane.*—In the same manner as above, the *copper salt* of 9 : 11-dioxodocosane was prepared as pale blue crystals, m. p. 85°, from sodium (10·2 g.), methyl undecyl ketone (39·6 g.), and ethyl nonanoate (74·4 g.; b. p. 227°) (Found: C, 72·0; H, 11·5. $C_{44}H_{82}O_4Cu$ requires C, 71·5; H, 11·2%).

This copper salt and cold hydrochloric acid (15%; 400 c.c.) ultimately gave a product, b. p. 230°/0·2 mm., which when crystallised from ethanol gave 9 : 11-*dioxodocosane* (30 g.), m. p. 45° (Found: C, 78·2; H, 12·6. $C_{22}H_{42}O_2$ requires C, 78·1; H, 12·4%).

Hydrolysis. 9 : 11-Dioxodocosane (2·2 g.) in sodium hydroxide (1%; 25 c.c.) was heated on the water-bath for 2 hr. and finally boiled for a few minutes. Extraction with ether yielded a solid (odour of methyl octyl ketone), but conversion into the 2 : 4-dinitrophenylhydrazone gave, on repeated recrystallisation, a product, m. p. 69° alone or when mixed with methyl undecyl ketone 2 : 4-dinitrophenylhydrazone, m. p. 69°. The absence of octyl undecyl ketone showed that the Adams and Hauser condensation had occurred on the methyl group of the methyl undecyl ketone. Moreover, concentration of the aqueous alkaline liquid, followed by acidification with concentrated hydrochloric acid, gave a soft solid which did not smell of acetic acid. Conversion into anilide, and several crystallisations, yielded a product, m. p. 74° alone or when mixed with the dodecananilide, m. p. 76°.

7 : 9-*Dioxopentadecane.*—From sodium (15·2 g.), hexyl methyl ketone (38·5 g.; b. p. 64°/18 mm.; n_D^{17} 1·4159), and ethyl heptanoate (95 g.), the *copper salt* of 7 : 9-dioxopentadecane was prepared as pale blue crystals, m. p. 115° (Found: C, 66·6; H, 10·0. $C_{30}H_{54}O_4Cu$ requires C, 66·5; H, 10·0%). Treatment with hydrochloric acid (20%; 500 c.c.) gave 7 : 9-*dioxopentadecane* (25 g.), b. p. 180—184°/17 mm., n_D^{23} 1·4640 (Found: C, 74·7; H, 11·5. $C_{15}H_{28}O_2$ requires C, 75·0; H, 11·7%).

9 : 11 : 19 : 21-*Tetraoxononacosane and Methyl* 9 : 11-*Dioxononadecanoate.*—From sodium (3·0 g., yielding 0·12 mole of $NaNH_2$), methyl octyl ketone (9·4 g., 0·06 mole; b. p. 90—94°/10

[5] Cole, *J.*, 1954, 3807. Cf., Wibley and Bunce, *Analyt. Chem.*, 1952, **24**, 623.

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mm., m. p. +2°), and dimethyl azelaate (13·4 g., 0·06 mole; n_D^{18} 1·4366; b. p. 143—150°/10 mm.) the *copper salt* of 9 : 11 : 19 : 21-tetraoxononacosane was prepared as pale blue crystals, m. p. 92° (Found: C, 66·0; H, 9·4. $C_{58}H_{100}O_8Cu_2$ requires C, 66·2; H, 9·5%).

Treatment of this salt with cold hydrochloric acid (20%; 120 c.c.) and crystallisation of the product from light petroleum (b. p. 40—60°) and from methanol, gave 9 : 11 : 19 : 21-*tetraoxononacosane* (4·5 g.) as plates, m. p. 66° (Found: C, 75·0; H, 11·3. $C_{29}H_{52}O_4$ requires C, 75·0; H, 11·2%).

A fraction, b. p. 178—182°/0·2 mm.. was also obtained, which, after extraction with methanol, gave *methyl* 9 : 11-*dioxononadecanoate* (0·5 g.) as crystals, m. p. 40° (Found: C, 70·5; H, 10·6. $C_{20}H_{38}O_4$ requires C, 70·6; H, 10·6%). However, when sodium (8·7 g., 0·36 mole of $NaNH_2$), dimethyl azelaate (74 g., 0·34 mole), and methyl octyl ketone (26·6 g., 0·17 mole) were used, the *copper salt* of methyl 9 : 11-dioxononadecanoate (74 g.) was obtained as pale blue crystals, m. p. 94° (Found: C, 64·7; H, 9·3. $C_{40}H_{70}O_8Cu$ requires C, 64·7; H, 9·4%). Treatment of this with cold hydrochloric acid (10%; 300 c.c.), followed by distillation, and extraction with light petroleum (b. p. 40—60°) gave methyl 9 : 11-dioxononadecanoate (21 g.; m. p. 40°), identical with the specimen obtained above.

Methyl 9 : 11-*Dioxoheptadecanoate and* 7 : 9 : 17 : 19-*Tetraoxopentacosane.*—In the same manner the *copper salt* of methyl 9 : 11-dioxoheptadecanoate was prepared as pale blue crystals, m. p. 82°, from sodium (5·1 g., 0·22 mole of $NaNH_2$), hexyl methyl ketone (12·8 g., 0·1 mole), and dimethyl azelaate (44·5 g., 0·2 mole) (Found: C, 62·8; H, 9·0. $C_{36}H_{62}O_8Cu$ requires C, 63·0; H, 9·0%). From this salt there was obtained, in the usual way, *methyl* 9 : 11-*dioxoheptadecanoate* (9 g.), a pale yellow oil, m. p. 3°, n_D^{19} 4677 (Found: C, 69·2; H, 10·4. $C_{18}H_{32}O_4$ requires C, 69·2; H, 10·3%).

The residue from the distillation yielded 7 : 9 : 17 : 19-*tetraoxopentacosane* (0·6 g.) as crystals, m. p. 54° (from light petroleum) (Found: C, 73·6; H, 10·7. $C_{25}H_{44}O_4$ requires C, 73·5; H, 10·8%).

9 : 11-*Dioxononadecanoic Acid.*—Methyl 9 : 11-dioxononadecanoate (2 g.), dilute hydrochloric acid (40 c.c.), and methanol (4 c.c.) were boiled under reflux for 24 hr., and then cooled. A solid separated on the surface and was removed by two extractions with ether (2 × 50 c.c.), Sodium hydrogen carbonate solution (5%; 20 c.c.) and dilute sodium carbonate (1 drop) were added to the ethereal solution and the mixture shaken vigorously for ½ hr. Sodium 9 : 11-dioxononadecanoate separated and was washed with a little ether and warmed with dilute hydrochloric acid. Ether extraction of the aqueous acid mixture and crystallisation of the product from 2-methylpentane gave 9 : 11-dioxononadecanoic acid (0·1 g.), needles, m. p. 57·8—58·6° alone, or when mixed with the dioxo-acid isolated by Faure and Smith [2] (Found: C, 69·9; H, 10·3. Calc. for $C_{19}H_{34}O_4$: C, 69·9; H, 10·5%).

9 : 11-*Dioxoheptadecanoic Acid.*—Similarly, methyl 9 : 11-dioxoheptadecanoate (2 g.), dilute hydrochloric acid (40 c.c.), and methanol (4 c.c.), boiled under reflux for 24 hr., yielded 9 : 11-*dioxoheptadecanoic acid* (0·7 g.) as plates, m. p. 49·8—50·0° (Found: C, 68·2; H, 10·0. $C_{17}H_{30}O_4$ requires C, 68·4; H, 10·1%). Surprisingly, this acid did not form a sparingly soluble sodium salt.

Pentadecane-7 : 9-*diol.*—7 : 9-Dioxopentadecane (10 g.) in methanol (10 c.c.) was added to potassium borohydride (3·2 g.) in aqueous methanol [6] (32 c.c. of methanol + 8 c.c. of water), and the mixture kept at room temperature for 24 hr. Dilution with water, neutralisation with dilute hydrochloric acid, extraction with ether, and recrystallisation from light petroleum (b. p. 40—60°) gave *pentadecane*-7 : 9-*diol* (1·9 g.), as needles, m. p. 91° (Found: C, 73·5; H, 12·9. $C_{15}H_{32}O_2$ requires C, 73·8; H, 13·1%). Unsaturated alcohols are probably also formed in the reduction.[7]

1 : 2-*Dihexylcyclopropane.*—Pentadecane-7 : 9-diol (1·8 g.) was refluxed with 50% w/v hydrogen bromide–acetic acid (50 c.c.) for 24 hr.; the mixture was then poured into water and extracted with ether, yielding a yellow liquid (2·6 g.) (Found: Br, 39·5. Calc. for $C_{15}H_{30}Br_2$: Br, 43·2%). The crude dibromide (2·5 g.) was refluxed with dry acetone (125 c.c.), sodium iodide (12·5 g.), and zinc dust (7·5 g.) for 6 hr.[4] The zinc dust was filtered off from the hot mixture and extracted with boiling chloroform (2 × 25 c.c.). The combined acetone and chloroform filtrates were poured into water and the whole was extracted with ether; the extract was

[6] Chaiken and W. G. Brown, *J. Amer. Chem. Soc.*, 1949, **71**, 122; Schlesinger, H. C. Brown, Hoekstra, and Rapp, *ibid.*, 1953, **75**, 199.

[7] Dreiding and Hartman, *ibid.*, p. 939.

washed with water, dried ($MgSO_4$), and evaporated. Distillation gave a product, b. p. 100—110° (bath)/0·5 mm., which was dissolved in light petroleum (b. p. 40—60°; 5 c.c.) and the solution poured on a column of acid-washed alumina (8 g.); the column was eluted with light petroleum (b. p. 40—60°; 50 c.c.). Evaporation of the first fraction (20 c.c.), 1 : 2-*dihexylcyclopropane* (0·8 g.), gave a liquid, free from bromine (Found: C, 85·2; H, 14·8. $C_{15}H_{30}$ requires C, 85·7; H, 14·3%). The infrared absorption showed bands at 3·27—3·30, and 9·83 μ (medium intensity).

Methyl 9 : 11-*Dihydroxyheptadecanoate*.—Methyl 9 : 11-dioxoheptadecanoate (7 g.) in methanol (10 c.c.) was added to sodium borohydride (1·8 g.) in methanol (20 c.c.). After a few minutes, a solution of sodium borohydride (1·8 g.) in water (10 c.c.) was added, and the whole kept at room temperature for 24 hr. The resulting solid yielded *methyl* 9 : 11-*dihydroxyheptadecanoate* (1·6 g.), m. p. 65° [from light petroleum (b. p. 60—80°)] (Found: C, 68·7; H, 11·6. $C_{18}H_{36}O_4$ requires C, 68·4; H, 11·4%). This ester (1·2 g.) was refluxed with 50% w/v hydrogen bromide–acetic acid (25 c.c.) for 24 hr. and the mixture worked up as above. The resulting liquid (1·4 g.) (Found: Br, 35·1. Calc. for $C_{18}H_{34}O_2Br_2$: Br, 36·2%), on debromination with zinc and sodium iodide in acetone as above, gave a colourless, bromine-free liquid (0·3 g.), b. p. 130° (bath temp.)/0·3 mm., showing in its infrared spectrum bands at 9·83 and 3·27—3·30 μ.

Methyl ω-(2-*Octylcyclopropyl*)*octanoate*.—Methyl 9 : 11-dioxononadecanoate (6 g.) was reduced with sodium borohydride to *methyl* 9 : 11-*dihydroxynonadecanoate* (1 g.), m. p. 78° (Found: C, 70·3, 69·7; H, 12·1, 11·2. $C_{20}H_{40}O_4$ requires C, 69·8; H, 11·6%). This ester (0·9 g.) on treatment with hydrogen bromide–acetic acid as described above gave a brown wax (1 g.) (Found: Br, 32·2. $C_{20}H_{38}O_2Br_2$ requires Br, 34·0%). Debromination with zinc and sodium iodide in acetone, as before except that the alumina column was eluted with ether, gave *methyl* ω-(2-*octylcyclopropyl*)*octanoate* (0·2 g.), as a liquid, b. p. 200° (bath temp.)/0·5 mm. (Found: C, 76·9; H, 12·5; Br, 0. $C_{20}H_{38}O_2$ requires C, 77·4; H, 12·3%). The infrared absorption spectrum showed a band at 3·27—3·30 μ and one of medium intensity at 9·8 μ.

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530. *The Reaction of Carbonyl Chloride with 1 : 2-Epoxides.*

By J. IDRIS JONES.

Carbonyl chloride (1 mole) adds readily to an epoxide (1 mole) with formation of the corresponding 2-chloro-substituted chloroformate. With 2 moles of epoxide and 1 mole of carbonyl chloride the product is the corresponding bis-2-chloroalkyl carbonate. The direction of ring opening in some unsymmetrical epoxides has been established: opening appears to be unidirectional. Series of 2-chloro-substituted carbamates and *N*-substituted carbamates have been prepared from the chloroformates, and a convenient synthesis of *N*-substituted oxazolid-2-ones has been evolved based on the removal of hydrogen chloride from the mono-*N*-substituted chloroalkyl carbamates. The chlorine atom in 2-chloro-1-phenylethyl carbamate is readily hydrolysed and elimination of ammonia follows, to give phenylethylene carbonate (2-oxo-4-phenyl-1 : 3-dioxolan). The reaction of thiocarbonyl chloride with epoxyethane has also been examined.

1 : 2-EPOXIDES are highly reactive and many of their reactions have been studied in detail.[1] When this work was undertaken [2] the reaction with carbonyl chloride had not been examined. With equimolar proportions it was found that ring opening occurs readily, with formation of 2-chloro-substituted chloroformates, but with 2 mol. of epoxide further

[1] Elderfield, "Heterocyclic Compounds," Wiley, 1950, Vol. I, pp. 1—57.
[2] "Chemistry Research," 1953, Department of Scientific and Industrial Research, p. 38.

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reaction ensues giving the corresponding bis-2-chloroalkyl carbonates in excellent yield. The latter reaction had been described by Pechukas.[3] Depending on the proportions of reactants and the experimental conditions it is possible to obtain high yields of either chloroformate or carbonate. In most cases the reaction is vigorous and exothermic, and cooling, or the use of an inert diluent, is necessary particularly if a catalyst, *e.g.*, pyridine, is added. Malinowski and Medjanzewa [4] recently reported that in ethyl bromide at 0° without a catalyst reaction proceeds only to the chloroformate stage and with only moderate yields.

When excess of carbonyl chloride was passed into liquid epoxyethane (ethylene oxide) containing a trace of pyridine at −10° to −20°, with cooling, and the temperature then allowed to rise slowly to room temperature, 2-chloroethyl chloroformate was obtained almost exclusively. (Pyridine and other tertiary bases are known to catalyse the decomposition of chloroformates [5] and, for this reason, it is advisable to use only minute amounts as catalyst if the end-product is to be the chloroformate.) When 2 mols. of the epoxide were similarly treated with 1 mol. of carbonyl chloride a quantitative yield of bis-2-chloroethyl carbonate resulted. The carbonate was also obtained in quantitative yield by treating 2-chloroethyl chloroformate with epoxyethane in the presence of a trace of pyridine. Vinyl chloroformate has been prepared by pyrolysis of glycol chloroformate [6] and the possibility that 2-chloroethyl chloroformate serves as an intermediate in this decomposition prompted a study of the pyrolysis of the chloroformate. Decomposition, however, proceeded almost exclusively to give ethylene dichloride. Attempts to prepare divinyl carbonate by removing hydrogen chloride from bis-2-chloroethyl carbonate with triethylamine and by pyrolysis at 450° were also unsuccessful.

1 : 2-Epoxy*cyclo*hexane reacted readily with carbonyl chloride, giving 2-chloro*cyclo*hexyl chloroformate and bis-2-chloro*cyclo*hexyl carbonate. If the usual Walden inversion occurs on ring opening, the chloroformate should have the *trans*-structure. This was confirmed by conversion of *trans*-2-chloro*cyclo*hexanol into the chloroformate by treatment with carbonyl chloride; the two products were identical. Two crystalline modifications of the carbonate, m. p.s 111° and 65—66° severally, were obtained. These correspond to the *meso*- and racemic forms of the *trans-trans*-carbonate, inversion occurring at each opening of the oxide ring.

1 : 2-Epoxypropane, being unsymmetrical, could give rise to two chloroformic esters according to the direction of ring opening. Thus, with hydrogen chloride, both 1-chloropropan-2-ol and 2-chloropropan-1-ol are formed.[7] However, under the conditions of our reaction the sole product was 2-chloro-1-methylethyl chloroformate. Its identity was established by comparison of its physical constants (including infrared absorption spectrum) with those of synthetic material prepared by an unequivocal method, *viz.*, by treating 1-chloropropan-2-ol (derived from allyl chloride by Bancroft's method [8]) with carbonyl chloride. Further, hydrolysis of the chloroformate obtained from the epoxide gave 1-chloropropan-2-ol, identical with the synthetic material. 1 : 2-Epoxypropane (2 mol.) and carbonyl chloride (1 mol.) gave di-(2-chloro-1-methylethyl) carbonate in excellent yield. There are two possible stereoisomeric forms of the carbonate, *meso* and racemic. On long storage one crystalline form (m. p. 50°) was obtained from the mixture. When 2-chloro-1-methylethyl chloroformate was condensed with 1-chloropropan-2-ol in equimolar proportions the mixed stereoisomeric carbonates obtained were the same as those derived from 1 : 2-epoxypropane.

In most reactions of 3-chloro-1 : 2-epoxypropane the oxide ring, although unsymmetrical, opens exclusively in one direction, and in the reaction with carbonyl chloride

[3] Pechukas, U.S.P. 2,518,058.
[4] Malinowski and Medjanzewa, *J. Gen. Chem.* (*U.S.S.R.*), 1953, **23**, 221.
[5] Nakanishi, Myers, and Jensen, *J. Amer. Chem. Soc.*, 1955, **77**, 5033.
[6] Küng, U.S.P. 2,377,085.
[7] Forsberg and Smith, *Acta Chem. Scand.*, 1947, **1**, 577.
[8] Bancroft, *J. Amer. Chem. Soc.*, 1919, **41**, 426.

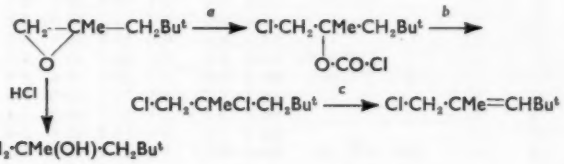
the only products were 2-chloro-1-chloromethylethyl chloroformate and di-(2-chloro-1-chloromethylethyl) carbonate. Attempts to prepare the chloroformate by treating 1 : 3-dichloropropan-2-ol with carbonyl chloride in an open system were unsuccessful, but the same carbonate, m. p. and mixed m. p. 47°, was obtained by heating 1 : 2-dichloropropan-2-ol with the chloroformate derived from the epoxide.

2-Chloroethyl 2-chloro-1-chloromethylethyl carbonate was prepared from 2-chloro-1-chloromethylethyl chloroformate and epoxyethane. This example serves to illustrate the preparation of mixed carbonates from chloroformic esters and epoxides.

2 : 3-Epoxybutane exists in *cis*- and *trans*-forms. The *trans*-form on treatment with carbonyl chloride gave the (±)-*erythro*-2-chloro-1-methylpropyl chloroformate. This structure was confirmed by the identity of the physical constants and infrared spectrum with those of material made from carbonyl chloride and (±)-*erythro*-2-chlorobutan-2-ol (prepared [9] by adding concentrated hydrochloric acid to *trans*-2 : 3-epoxybutane). The corresponding carbonate was also obtained, presumably, as a mixture of stereoisomers.

The chloroformate derived from styrene oxide proved to be exclusively (±)-2-chloro-1-phenylethyl chloroformate. The related carbonate was obtained as a mixture of two stereoisomeric forms, one of which was crystalline.

Attempts to prepare the chloroformate from 1 : 2-epoxy-2 : 4 : 4-trimethylpentane were unsuccessful. Decomposition intervened and the only products characterised were 1-chloro-2 : 4 : 4-trimethylpentan-2-ol, identical with the isomer described by Graham, Millidge, and Young,[10] and a chlorotrimethylpentene, presumably 1-chloro-2 : 4 : 4-trimethylpent-2-ene which appears to be identical with that described by Umnowa [11] as resulting from the reaction of chlorine or hypochlorous acid with di*iso*butene and by Graham *et al.*[10] as a product of dehydration of the chlorohydrin. The reaction with carbonyl chloride is believed to take the following course :



The hydrogen chloride liberated in reaction (*c*) reacts with the epoxide, giving the chlorohydrin.

The infrared absorption spectra of the chloroformates and carbonates prepared have already been reported.[12] The chloroformates have been used for synthesising a series of chlorocarbamates and *N*-substituted chlorocarbamates for screening as selective weed-killers (see Table 1).

In 1885 Nemirowsky [13] prepared 2-chloroethyl *N*-phenylcarbamate from 2-chloroethyl chloroformate (derived from carbonyl chloride and 2-chloroethanol) and found it to cyclise readily in alkaline solution to give 3-phenyloxazolid-2-one. Other 2-chloroethyl carbamates and oxazolidones have been prepared in the same way by others.[14] Delaby *et al.*[15] prepared 2-chloroethyl carbamates by the reaction of thionyl chloride on the corresponding 2-hydroxyethyl carbamates, and Chabrier *et al.*[16] extended this reaction.

[9] Lucas and Gould, *J. Amer. Chem. Soc.*, 1941, **63**, 2547.
[10] Graham, Millidge, and Young, *J.*, 1954, 2180.
[11] Umnowa, *J. Russ. Phys. Chem. Soc.*, 1910, **42**, 1536.
[12] Hales, Jones, and Kynaston, *J.*, 1957, 618.
[13] Nemirowsky, *J. prakt. Chem.*, 1885, **31**, 173.
[14] (*a*) Otto, *ibid.*, 1891, **44**, 15; (*b*) Johnson and Langley, *Amer. Chem. J.*, 1910, **44**, 352; (*c*) Adams and Segur, *J. Amer. Chem. Soc.*, 1923, **45**, 785; (*d*) Pierce, *ibid.*, 1928, **50**, 241; (*e*) Sprinson, *ibid.*, 1941, **63**, 2249; (*f*) McKay and Braun, *J. Org. Chem.*, 1951, **16**, 1829.
[15] Delaby, Sekera, Chabrier, and Piganiol, *Bull. Soc. chim. France*, 1951, 392.
[16] Chabrier, Najer, and Giudicelli, *Compt. rend.*, 1954, **238**, 1593.

TABLE 1.

X	Yield (%)	M. p.	B. p. (°/mm.)	Found (%) C	H	N	Cl	Required (%) C	H	N	Cl	Refs.
2-Chloroethyl carbamates, $Cl\cdot CH_2\cdot CH_2\cdot O\cdot CO\cdot X$												
NH_2	97	77°	—	29·5	4·9	11·3	28·5	29·2	4·9	11·3	28·7	15
NHMe	90	19	111°/13	35·1	5·9	10·3	25·3	34·9	5·8	10·2	25·8	14*e*, 15
NHEt	88	23	115—118°/19	39·4	6·8	8·5	23·3	39·6	6·6	9·2	23·4	14*e*, 15
NHBu^n	80	—	142—145°/16	46·8	7·8	7·8	19·6	46·8	7·8	7·8	19·7	14*e*
$NH\cdot C_5H_{11}$-*n*	76	—	87—88°/0·25	49·2	8·4	7·5	18·5	49·6	8·3	7·2	18·3	
$NH\cdot C_6H_{13}$-*n*	77	21·5	102—103°/0·25	52·2	8·8	7·4	17·0	52·0	8·7	6·7	17·1	
$NH\cdot C_7H_{15}$-*n*	70	19	120°/0·35	54·5	9·4	6·6	16·1	54·2	9·1	6·3	16·0	
$NH\cdot C_8H_{17}$-*n*	52	27·5	135—136°/0·15	55·9	9·3	5·8	15·0	56·1	9·4	5·9	15·0	
NHPh	91	52	148—150°/1	54·0	5·0	6·9	17·7	54·1	5·0	7·0	17·8	13, 14*e*
$NH\cdot C_6H_4Me$-*p*	88	62	168—170°/1	56·3	5·8	6·5	16·4	56·2	5·7	6·6	16·6	14*c*
$NH\cdot C_6H_4Me$-*o*	73	49	—	56·6	5·8	6·4	16·6	56·2	5·7	6·6	16·6	14*c*, *f*
$NH\cdot C_6H_4Cl$-*o*	92	58·5	—	46·6	4·0	6·3	29·6	46·0	4·3	6·0	30·2	14*c*, *f*
$NH\cdot C_6H_4Cl$-*m*	83	50	—	46·2	3·9	5·9	30·0	46·0	4·3	6·0	30·2	14*f*
$NH\cdot C_6H_4Cl$-*p*	95	72	—	46·2	3·9	6·1	29·9	46·0	4·3	6·0	30·2	14*c*, *f*
$NH\cdot C_{10}H_7$-α	77	105	—	62·4	4·8	5·9	14·2	62·5	4·8	5·6	14·2	14*a*, *f*
$NH\cdot C_{10}H_7$-β	77	103·5	—	62·6	4·9	5·4	14·8	62·5	4·8	5·6	14·2	14*a*
NEt_2	87	—	109—110°/15	46·8	7·8	7·7	19·5	46·8	7·8	7·8	19·7	14*e*, *f*
NPh_2	75	77	—	65·5	5·1	4·8	12·7	65·3	5·1	5·1	12·9	
NPhMe	82	—	112—115°/0·1	55·8	5·6	7·0	16·5	56·2	5·6	6·6	16·6	
$N<[CH_2]_5$	84	—	101—102°/0·1	49·2	7·1	7·0	19·2	50·1	7·3	7·3	18·5	14*e*
2-Chloro-1-methylethyl carbamates, $Cl\cdot CH_2\cdot CHMe\cdot O\cdot CO\cdot X$												
NH_2	95	63	—	34·7	5·7	10·1	26·0	34·9	5·8	10·2	25·8	16
NHMe	92	—	116°/15	39·3	6·7	9·0	22·9	39·6	6·6	9·2	23·4	16
NHBu^n	83	—	145°/15	49·8	8·5	7·1	18·3	49·6	8·3	7·2	18·3	
$NH\cdot C_5H_{11}$-*n*	72	—	97—99°/0·15	52·0	8·7	7·1	18·1	52·0	8·7	6·7	17·1	
$NN\cdot C_6H_{13}$-*n*	85	1	112—114°/0·2	54·6	9·2	6·9	16·0	54·2	9·1	6·3	16·0	
$NH\cdot C_7H_{15}$-*n*	50	5	130—135°/0·3	55·8	9·5	5·8	15·6	56·1	9·4	5·9	15·0	
$NH\cdot C_8H_{17}$-*n*	64	9	120—121°/0·15	57·5	9·8	5·7	14·9	57·7	9·7	5·6	14·2	
NHPh	95	37	145°/0·1	56·6	5·7	7·1	16·0	56·2	5·7	6·6	16·6	
$NH\cdot C_6H_4Me$-*o*	81	53	—	58·0	6·3	6·7	15·7	58·0	6·2	6·2	15·6	
$NH\cdot C_6H_4Me$-*p*	97	55	—	58·0	6·4	6·6	15·5	58·0	6·2	6·2	15·6	
$NH\cdot C_6H_4Cl$-*o*	92	—	122°/0·25	48·9	4·8	6·0	28·2	48·4	4·5	5·7	28·6	
$NH\cdot C_6H_4Cl$-*m*	83	—	150—155°/0·1	48·2	4·2	5·8	29·1	48·4	4·5	5·7	28·6	
$NH\cdot C_6H_4Cl$-*p*	93	65·5	—	48·4	4·5	6·4	28·6	48·4	4·5	5·7	28·6	
$NH\cdot C_{10}H_7$-α	72	71	—	64·5	5·4	5·1	13·5	63·8	5·4	5·3	13·5	
$NH\cdot C_{10}H_7$-β	89	102·5	—	63·8	5·4	5·8	13·4	63·8	5·4	5·3	13·5	
NEt_2	73	—	110—111°/16	49·6	8·15	7·2	18·4	49·6	8·3	7·2	18·3	
2-Chloro-1-chloromethylethyl carbamates, $(Cl\cdot CH_2)_2CH\cdot O\cdot CO\cdot X$												
NH_2	80	84	—	28·0	4·0	8·3	41·2	27·9	4·1	8·1	41·2	14*a*
NHMe	89	20	105—107°/0·2	32·4	4·6	7·3	38·4	32·3	4·9	7·5	38·1	
NHPh	89	78	—	48·4	4·5	5·6	28·7	48·4	4·5	5·7	28·6	14*a*
$NH\cdot C_6H_4Me$-*o*	87	72	—	50·7	4·9	5·9	26·9	50·4	5·0	5·3	27·0	
$NH\cdot C_6H_4Cl$-*o*	86	63	—	42·9	3·6	5·3	37·4	42·5	3·6	5·0	37·7	
$NH\cdot C_6H_4Cl$-*m*	92	72·5	—	43·0	3·7	5·2	37·4	42·5	3·6	5·0	37·7	
$NH\cdot C_6H_4Cl$-*p*	77	111	—	42·8	3·6	5·2	35·0	42·5	3·6	5·0	37·7	
$NH\cdot C_{10}H_7$-α	91	121	—	56·2	4·2	5·0	24·0	56·4	4·4	4·7	23·8	14*a*
$NH\cdot C_{10}H_7$-β	90	104·5	—	56·3	4·2	4·7	23·4	56·4	4·4	4·7	23·8	14*a*
NMe_2	97	—	102—104°/0·15	35·9	5·6	6·7	35·4	36·0	5·5	7·0	35·5	
NEt_2	63	—	112—115°/0·15	42·1	6·5	6·1	31·4	42·1	6·6	6·1	31·1	
2-Chloro-1-phenylethyl carbamates, $Cl\cdot CH_2\cdot CHPh\cdot O\cdot CO\cdot X$												
NH_2	98	71	—	54·15	4·8	7·0	17·8	54·15	5·0	7·0	17·8	
NHMe	84	53	—	56·3	5·7	6·5	16·8	56·2	5·7	6·6	16·6	
NHEt	80	—	141—142°/0·15	60·3	6·4	5·5	16·2	58·0	6·2	6·2	15·6	
NHPh	99	94·5	—	65·1	5·1	5·3	13·1	65·3	5·1	5·1	12·9	
$NH\cdot C_6H_4Cl$-*p*	96	96	—	58·0	4·2	4·3	22·3	58·1	4·2	4·5	22·9	
NMe_2	90	—	138—139°/0·15	58·4	6·4	5·7	15·5	58·0	6·2	6·2	15·6	
(±)-erythro-*2-Chloro-1-methylpropyl carbamates*, $CHClMe\cdot CHMe\cdot O\cdot CO\cdot X$												
NH_2	96	67·5	—	39·7	6·4	9·0	23·6	39·4	6·6	9·2	23·3	
NHMe	65	—	120°/16	43·7	7·2	8·5	21·3	43·5	7·3	8·5	21·4	
NHPh	77	66	—	58·1	5·8	5·8	15·9	58·0	6·15	6·15	15·6	
trans-*2-Chlorocyclohexyl carbamates*, $C_6H_{10}Cl\cdot O\cdot CO\cdot X$												
NH_2	92	150	—	47·5	6·8	7·9	19·9	47·3	6·8	7·9	20·0	
NHMe	92	56	161°/16	50·3	7·4	7·4	18·5	50·1	7·4	7·3	18·5	

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TABLE 2. 3-R^1-5-R^2-*Oxazolid*-2-*ones*.

		Yield		Found (%)				Required (%)			
R^1	R^2	(%)	M. p.	C	H	N	Cl	C	H	N	Cl.
Ph	Ph	97	129°	75·0	5·4	5·9	—	75·3	5·4	5·9	—
Ph	CH_2Cl	95	108	56·5	4·8	6·4	16·6	56·7	4·7	6·6	16·8
β-$C_{10}H_7$	Me	95	134	73·8	5·7	6·2	—	74·0	5·7	6·2	—
p-C_6H_4Me	Me	93	67·5	68·9	6·7	7·3	—	69·1	6·8	7·3	—
p-C_6H_4Cl	CH_2Cl	93	126·5	48·8	3·6	6·2	28·5	48·8	3·7	5·7	28·8
p-C_6H_4Cl	Ph	96	131	65·8	4·5	5·1	13·0	65·8	4·4	5·1	12·9
p-C_6H_4Cl	Me	94	114	56·6	4·7	6·7	16·4	56·7	4·7	6·6	16·8
p-C_6H_4Cl	H	92	122·5	54·9	4·1	7·1	17·7	54·7	4·1	7·1	18·0
m-C_6H_4Cl	H	95	55	54·5	4·1	7·0	18·0	54·7	4·1	7·1	18·0

An attempt by Boberg and Schultze [17] to condense epoxides with carbamoyl chloride gave only the chlorohydrins. While the 2-chloroalkyl *N*-monosubstituted carbamates are readily converted into *N*-substituted oxazolidones it was not possible to synthesise the parent oxazolidones from the unsubstituted carbamates. When 2-chloroethyl carbamate was treated with 1 mol. of alcoholic alkali breakdown occurred with formation of alkali cyanide and chloride and some epoxide. A similar observation has been reported by Delaby *et al.*[15]

Hexahydrobenzoxazolid-2-one and its *N*-methyl derivative, the *cis*- and the *trans*-form of which have been reported by Mousseron *et al.*,[18] could not be prepared by treatment of *trans*-2-chloro*cyclo*hexyl carbamate and its *N*-methyl derivative with alcoholic alkali. The *N*-substituted oxazolid-2-ones we prepared from the *N*-substituted chlorocarbamates are listed in Table 2. The availability of the 2-chloro-substituted chloroformates from the epoxide–carbonyl chloride reaction makes this approach to the synthesis of *C*- and *N*-substituted oxazolidones attractive.

Crystallisation of 2-chloro-1-phenylethyl carbamate from methanol gave phenylethylene carbonate (2-oxo-4-phenyl-1 : 3-dioxolan) and ammonium chloride. An attempt to prepare the carbamate with concentrated aqueous ammonia also led to the formation of phenylethylene carbonate. The reaction in methanol was found to be due to its water content. The chlorine atom of the carbamate is hydrolysed readily in water and cyclisation of the 2-hydroxy-1-phenylethyl carbamate follows with loss of ammonia. 2-Hydroxyethyl carbamate, which is readily prepared from ethylene carbonate and concentrated aqueous ammonia, is stable even at the boiling point.

The reaction of thiocarbonyl chloride with epoxyethane was also examined. Even in the presence of pyridine the reaction does not proceed very readily at room temperature and the 2-chloroethyl chlorothioformate which is initially formed decomposes on distillation to give ethylene dichloride and carbonyl sulphide. Some bis-2-chloroethyl thiocarbonate was also formed in the reaction, and the infrared absorption spectrum indicates that this is present as a mixture of bis-2-chloroethyl thiol- and thion-carbonates.

EXPERIMENTAL

Reaction of Carbonyl Chloride with Epoxyethane.—Over a period of 1¼ hr. carbonyl chloride (65·9 g.) was passed into epoxyethane (35·5 g.) containing 3 drops of pyridine, held at $< -10°$ by an acetone–carbon dioxide bath. The temperature was allowed to rise to room temperature overnight, and dry air was blown through the product until the weight was constant (98 g.). On fractional distillation the mixture afforded 2-chloroethyl chloroformate (83 g.), b. p. 153°/760 mm., 50°/15 mm., n_D^{20} 1·4460, and bis-2-chloroethyl carbonate (11 g.), m. p. 11°, b. p. 241°/760 mm., 125°/12 mm., n_D^{20} 1·4600.

When epoxyethane (195 g.) containing 3 drops of pyridine was treated with carbonyl chloride (335 g.) during 3 hr. at −30°, treatment as above gave a final weight increase of 329 g. and then 2-chloroethyl chloroformate (440 g.), n_D^{20} 1·4460, and 33 g. of the carbonate.

[17] Boberg and Schultze, *Chem. Ber.*, 1955, **88**, 275.
[18] Mousseron, Winternitz and Mousseron-Canet, *Bull. Soc. chim. France*, 1953, 737.

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Bis-2-chloroethyl carbonate (188 g.), b. p. 131°/15 mm., was obtained as sole product when epoxyethane (100 g.) containing 2 drops of pyridine was treated at −15° to −20° with carbonyl chloride (101 g.) and left without further cooling for 24 hr., after which a slight excess of the epoxide was removed in a stream of air. A quantitative yield of bis-2-chloroethyl carbonate was also obtained by passing epoxyethane into 2-chloroethyl chloroformate (containing a trace of pyridine) at <0° until the required gain in weight had been attained.

Pyrolysis of 2-Chloroethyl Chloroformate and Bis-2-chloroethyl Carbonate.—During 2 hr. 2-chloroethyl chloroformate (25 g.) was swept with a stream of carbon dioxide through a glass tube packed with broken porous pot and kept at 450°, then through a water-condenser and a cold trap at −80°. The total condensate (9·8 g.), b. p. 81—83°, m. p. −39° to −41°, n_D^{20} 1·4428, proved to be substantially ethylene dichloride. When bis-2-chloroethyl carbonate (25 g.) was pyrolysed at 450° (3¾ hr.), 16·4 g. of liquid condensate were mostly unchanged material (15 g.), b. p. 130°/14 mm., n_D^{20} 1·4595. Attempts to prepare divinyl carbonate by treating bis-2-chloroethyl carbonate (18·7 g.) in dry ether (50 ml.) with triethylamine (10·5 g.) were unsuccessful: no reaction was observed even on prolonged refluxing or in the absence of the solvent. Treatment with alcoholic potassium hydroxide caused hydrolysis of the carbonate as well as some elimination of hydrogen chloride.

Reaction of Carbonyl Chloride with 1 : 2-*Epoxy*cyclo*hexane.*—At ~−10° 1 : 2-epoxy*cyclo*hexane [19] (21 g. + 2 drops of pyridine) was treated with carbonyl chloride (16 g.). After being kept overnight, without further cooling, the liquid product was fractionated. It yielded 2-*chloro*cyclo*hexyl chloroformate* (27 g.), b. p. 110—111°/13 mm., n_D^{25} 1·4775 (Found: C, 42·7; H, 5·0; Cl, 35·8. $C_7H_{10}O_2Cl_2$ requires C, 42·6; H, 5·1; Cl, 36·8%), and a viscous carbonate fraction (9·6 g.), b. p. 177—183°/0·7 mm., which solidified and on fractional crystallisation from ethanol and then from light petroleum (b. p. 60—80°) yielded two *isomers* of *bis*-2-*chloro*cyclo*hexyl carbonate*, m. p. 111° (Found: C, 52·9; H, 6·8; Cl, 23·9. $C_{13}H_{20}O_3Cl_2$ requires C, 52·9; H, 6·8; Cl, 24·0%) and 65—66° (Found: C, 53·0; H, 6·9; Cl, 23·6%). Infrared examination of the two compounds showed only very minor differences, that could well be expected of stereoisomers.

1 : 2-Epoxy*cyclo*hexane and excess of carbonyl chloride at −20° with no catalyst gave exclusively the chloroformate, b. p. 114—114·5°/16 mm.

trans-2-Chloro*cyclo*hexanol was prepared by addition of hypochlorous acid to *cyclo*hexene.[20] The chlorohydrin, n_D^{20} 1·4891, crystallised (m. p. 25°, not hitherto recorded). Carbonyl chloride was passed into the chlorohydrin (20 g.) at 100° until the gain in weight after removal of dissolved carbonyl chloride was 7 g. Distillation afforded unchanged chlorohydrin and some chloroformate (10·5 g.). The recovered chlorohydrin was again treated with carbonyl chloride (3 hr.) and furnished more chloroformate (7·1 g.). Further treatment of the unchanged material gave still more chloroformate (3·2 g.). Redistillation of the combined chloroformate fractions (20·8 g.) gave trans-2-*chloro*cyclo*hexyl chloroformate* (18 g.), n_D^{25} 1·4778, b. p. 114—115°/16 mm., whose infrared absorption was identical with that of the above chloroformate derived from 1 : 2-epoxy*cyclo*hexane.

There was no reaction when *trans*-2-chloro*cyclo*hexyl chloroformate (3·3 g.) and *trans*-2-chloro*cyclo*hexanol (2·3 g.) were heated for 4½ hr. at 100°. At 150° decomposition intervened.

Reaction of Carbonyl Chloride with 1 : 2-*Epoxypropane.*—Carbonyl chloride (211 g.) was passed into 1 : 2-epoxypropane (116 g.) containing 3 drops of pyridine at <−20° (carbon dioxide–acetone). Treatment as above gave 2-chloro-1-methylethyl chloroformate (305 g.), b. p. 59—60°/16 mm., n_D^{20} 1·4420 (Found: C, 30·8; H, 4·0; Cl, 44·8. Calc. for $C_4H_6O_2Cl_2$: C, 30·5; H, 3·85; Cl, 45·1%) (Malinowski and Medjanzewa [4] give b. p. 68—70°/70 mm., n_D^{18} 1·4462).

1-Chloropropan-2-ol,[8] b. p. 126—127°, n_D^{20} 1·4370, on treatment with carbonyl chloride gave the same chloroformate, b. p. 58—59°/15 mm., n_D^{20} 1·4419. The infrared spectra were identical. Further, the chloroformate derived from the epoxide furnished on hydrolysis 1-chloropropan-2-ol, b. p. 125—128°, n_D^{20} 1·4374.

1 : 2-Epoxypropane (40 g.) containing 2 drops of pyridine, when treated with carbonyl chloride (54 g.) at −10° to −20° and kept for 48 hr., furnished a 97·5% yield of *di*-(2-*chloro*-1-*methylethyl*) *carbonate*, b. p. 133°/16 mm., n_D^{20} 1·4522 (Found: C, 39·2; H, 5·6; Cl, 33·0. $C_7H_{12}O_3Cl_2$ requires C, 39·1; H, 5·6; Cl, 33·0%). After several months about half the material crystallised [m. p. 50° after crystallisation three times from light petroleum (b. p. 60—80°)].

[19] *Org. Synth.*, Coll. Vol. I, Wiley, 1947, p. 185.
[20] See ref. 19, p. 158.

The same carbonate, b. p. 133°/15 mm., n_D^{20} 1·4518, presumably as a mixture of stereoisomers, was obtained by heating equimolar proportions of 2-chloro-1-methylethyl chloroformate and 1-chloropropan-2-ol.

Reaction of Carbonyl Chloride with 3-*Chloro*-1 : 2-*epoxypropane.*—3-Chloro-1 : 2-epoxypropane (20·7 g.) with 2 drops of pyridine was treated with a slow stream of carbonyl chloride at room temperature for 1 hr. at >40°. After removal of dissolved carbonyl chloride the gain in weight was 21·8 g. Fractional distillation gave 2-chloro-1-chloromethylethyl chloroformate (10 g.), b. p. 93°/20 mm., n_D^{20} 1·4740 (Found : C, 25·3; H, 2·7; Cl, 55·3. Calc. for $C_4H_5O_2Cl_3$: C, 25·1; H, 2·6; Cl, 55·6%), and *di*-(2-*chloro*-1-*chloromethylethyl*) *carbonate* (25 g.), m. p. 47·5°, b. p. 185°/22 mm. (Found : C, 29·6; H, 3·6; Cl, 50·0. $C_7H_{10}O_3Cl_4$ requires C, 29·6; H, 3·5; Cl, 49·9%). Otto [14] described the preparation of the chloroformate from 1 : 3-dichloropropan-2-ol and carbonyl chloride at 170° in 24 hr. When the dichlorohydrin (20 g.) was treated with a two-fold excess of liquid carbonyl chloride at −10° and the temperature allowed to rise slowly to room temperature no appreciable reaction was observed. Nor was chloroformate obtained by passing carbonyl chloride for 3 hr. into a refluxing solution of the dichlorohydrin (25 g.) in carbon tetrachloride (50 g.). Di-(2-chloro-1-chloromethylethyl) carbonate (24 g.), m. p. 47·5°, was obtained by refluxing the chloroformate (19 g.) with the dichlorohydrin (13 g.) for 2 hr., followed by distillation *in vacuo*. There was no depression in m. p. on admixture with the carbonate obtained from *epi*chlorohydrin and carbonyl chloride.

2-*Chloroethyl* 2-*Chloro*-1-*chloromethylethyl Carbonate.*—Epoxyethane was passed into 2-chloro-1-chloromethylethyl chloroformate (50 g.) containing 2 drops of pyridine until the gain in weight due to combined epoxide was 10·8 g. Some cooling (ice-water) was necessary in the early stages of the reaction. On fractional distillation 2-*chloroethyl* 2-*chloro*-1-*chloromethylethyl carbonate* (53·5 g., 87%), b. p. 152°/13 mm., n_D^{20} 1·4798 (Found : C, 30·8; H, 3·85; Cl, 45·1. $C_6H_9O_3Cl_3$ requires C, 30·6; H, 3·85; Cl, 45·2%), was obtained.

Reaction of Carbonyl Chloride with trans-2 : 3-*Epoxybutane.*—(±)-*trans*-2 : 3-Epoxybutane, b. p. 53·5°, n_D^{20} 1·3729 (36 g. + 3 drops of pyridine), was cooled to −20° and carbonyl chloride (62 g.) passed in during 1½ hr. Next morning working up gave a final increase in weight of 34 g. Two other batches of epoxide, each weighing 36 g., with catalyst were similarly treated. The final weight increases were 30 g. and 24 g. The three liquid products were combined and fractionated through a column (60 × 1 cm.) packed with glass helices, with a reflux ratio of 25 : 1. Material (19·6 g.) of b. p. >64·4°/16 mm. was redistilled twice and gave *di*-(2-*chloro*-1-*methylpropyl*) *carbonate* (17·6 g.), b. p. 134—135°/16 mm. (Found : C, 44·9; H, 6·6; Cl, 28·8. $C_9H_{14}O_3Cl_2$ requires C, 44·5; H, 6·6; Cl, 29·2%), presumably as a mixture of its stereoisomers. Material (53·3 g.), b. p. 61·6—64·4°/16 mm., was refractionated, giving fractions (1) b. p. 61·6—62·4°/16 mm., n_D^{20} 1·4412, (2) b. p. 62·4—63·2°/16 mm., n_D^{20} 1·4417, (3) b. p. 63·2—63·4°/16 mm., n_D^{20} 1·4422, (4) b. p. 63·4—64·0°/16 mm., n_D^{20} 1·4421.

Fraction (3) (17·2 g.) was pure (±)-erythro-2-*chloro*-1-*methylpropyl chloroformate* (cf. below) (Found : C, 35·4; H, 4·7; Cl, 41·2. $C_5H_8O_2Cl_2$ requires C, 35·1; H, 4·7; Cl, 41·5%). The stereochemical configuration was established by converting (±)-*erythro*-3-chlorobutan-2-ol [9] (24 g.) by carbonyl chloride (2 hr.) into the same chloroformate (25·4 g.), b. p. 62·5—63·5°/15 mm., n_D^{25} 1·4400, with an identical infrared spectrum.

trans-2 : 3-Epoxybutane (36 g. + 2 drops of pyridine) when treated at −10° absorbed 25 g. of carbonyl chloride (final gain 23 g.). Distillation gave main fractions (1) b. p. 46°/15 mm. (17 g.), n_D^{20} 1·4460, (2) chloroformate (19 g.), b. p. 63°/15 mm., n_D^{20} 1·4410, and (3) carbonate (12 g.), b. p. 134—135°/16 mm., n_D^{20} 1·4500.

Reaction of Carbonyl Chloride with Epoxyphenylethane (*Styrene Oxide*).—To obtain a high yield of the chloroformate it was necessary to add epoxyphenylethane (24 g.) to excess of carbonyl chloride (60 g.) containing 3 drops of pyridine at −20° and then to allow the temperature to rise slowly. After removal of excess carbonyl chloride 43 g. of liquid remained. Decomposition set in at ~140° during the distillation of the product under water-pump pressure but, at a lower pressure, distillation furnished (±)-2-*chloro*-1-*phenylethyl chloroformate* (35·2 g.), b. p. 109°/0·15 mm. (Found : C, 49·4; H, 3·7; Cl, 32·2. $C_9H_8O_2Cl_2$ requires C, 49·35; H, 3·7; Cl, 32·4%). On hydrolysis the chloroformate gave (±)-2-chloro-1-phenylethanol, b. p. 128°/16 mm., n_D^{20} 1·5400.

Addition of 1 drop of pyridine to a mixture of 2-chloro-1-phenylethyl chloroformate (4·38 g.) and epoxyphenylethane (2·4 g.) caused an immediate rise in temperature. Reaction was completed in 2 hr. on the steam-bath. The product partly crystallised and the solid fraction

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after several crystallisations from light petroleum (b. p. 60—80°)–chloroform furnished one of the two stereoisomeric forms of *di*-(2-*chloro*-1-*phenylethyl*) *carbonate*, m. p. 51° (Found : C, 60·0; H, 4·75; Cl, 20·8. $C_{17}H_{16}O_3Cl_2$ requires C, 60·2; H, 4·75; Cl, 20·9%). The same mixture (16·9 g.) was obtained by treating epoxyphenylethane (12 g.), containing 3 drops of pyridine, at −20° with carbonyl chloride (6 g.). Seeding induced separation of the isomer, m. p. and mixed m. p. 51°.

Reaction of Carbonyl Chloride with 1 : 2-*Epoxy*-2 : 4 : 4-*trimethylpentane*.—Carbonyl chloride (116 g.) was added during ½ hr. at −10° to the epoxide (128 g.) containing 4 drops of pyridine. After 12 hr., during which room temperature was attained, and removal of dissolved carbonyl chloride, only 26 g. remained combined. More was passed in at room temperature until the weight increase was 80 g. On distillation of the product it was difficult to maintain the vacuum owing to decomposition. The distillate (136 g.) obtained at 16—18 mm. had a wide boiling range and was refractionated; it gave eight fractions. One (37·1 g.), b. p. 78—81°/16 mm., n_D^{20} 1·4511 (Found : C, 58·8; H, 10·3; Cl, 21·7. Calc. for $C_8H_{17}OCl$: C, 58·4; H, 10·3; Cl, 21·6%), was probably 1-chloro-2 : 4 : 4-trimethylpentan-2-ol (cf. Graham *et al.*[10]). Another (11·8 g.), b. p. 50—52°/16 mm., n_D^{20} 1·4468, was probably slightly impure 1-chloro-2 : 4 : 4-trimethylpent-2-ene (Found : C, 66·2; H, 10·7; Cl, 23·1. Calc. for $C_8H_{15}Cl$: C, 65·5; H, 10·3; Cl, 24·2%) (cf. refs. 10 and 11). No fraction corresponded to a chloroformate.

Preparation of Carbamates from Chloroformates.—The series of 58 carbamates detailed in Table 1 were prepared in the prescribed manner from the appropriate chloroformate (1 mol.) with ammonia or primary or secondary amine (2 mol.), usually in benzene. The hydrochlorides were removed by filtration and the carbamates were isolated from the benzene and distilled or crystallised from light petroleum (b. p. 60—80°)–chloroform.

Hydrolysis of 2-*Chloro*-1-*phenylethyl Carbamate. Preparation of Phenylethylene Carbonate* (2-*Oxo*-4-*phenyl*-1 : 3-*dioxolan*).—Gaseous ammonia was passed into a solution of 2-chloro-1-phenylethyl chloroformate (5 g.) in dry benzene (50 ml.). The solution became warm and ammonium chloride (1·15 g.) when completely precipitated was removed and washed with benzene. The product recovered from the benzene solution was 2-*chloro*-1-*phenylethyl carbamate* (4·6 g.), m. p. 71° [from light petroleum (b. p. 60—80°)–chloroform] (for analysis see Table). Treatment with boiling water gave an oil which solidified. Crystallisation of the latter from aqueous ethanol gave *phenylethylene carbonate*, m. p. 54—56° (Found : C, 65·75; H, 4·9. $C_9H_8O_3$ requires C, 65·85; H, 4·9%). Its structure was confirmed by comparison of its infrared absorption spectrum with those of epoxyphenylethane and ethylene carbonate.[12] Crystallisation of 2-chloro-1-phenylethyl carbamate from methanol also gave phenylethylene carbonate and ammonium chloride. Treatment of the chloroformate with concentrated aqueous ammonia gave phenylethylene carbonate directly.

Synthesis of Oxazolid-2-*ones from* N-*Substituted Carbamates*.—Treatment of the unsubstituted carbamates (1 mol.) with alcoholic potassium hydroxide (1 mol.) caused formation of some potassium cyanate, potassium chloride, and epoxide. This was true, *e.g.*, of 2-chloroethyl carbamate, *trans*-2-chloro*cyclo*hexyl carbamate and *trans*-2-chloro*cyclo*hexyl *N*-methyl carbamate. Thus, an attempt to prepare hexahydro-3-methylbenzoxazolid-2-one from it was unsuccessful. With these exceptions elimination of hydrogen chloride from *N*-monosubstituted carbamates occurred readily with formation of 3-substituted oxazolid-2-ones. The general procedure adopted for the preparation of the oxazolidones listed in Table 2 was to add the appropriate amount of an ~10% ethanolic solution of potassium hydroxide to the requisite amount of carbamate in 10% ethanol solution. Precipitation of potassium chloride was almost immediate but the reaction was completed by heating for a few minutes at 100°. Because of the somewhat low solubility of some of the oxazolidones the potassium chloride was removed by filtering the hot solution and was washed with alcohol.

Reaction of Epoxyethane with Thiocarbonyl Chloride.—Epoxyethane (13·3 g.) was passed into thiocarbonyl chloride (23 g.) containing 2 drops of pyridine at 0°. After 24 hr. at room temperature the mixture was distilled. Some unchanged epoxyethane was recovered together with some thiocarbonyl chloride. When the temperature had reached 70° an exothermic reaction set in causing violent ebullition. When this stopped the liquid residue was distilled under reduced pressure and gave a pale yellow liquid (4·8 g.). This was redistilled and gave a constant-boiling fraction (4·2 g.), b. p. 127°/13 mm., n_D^{20} 1·5031 (Found : C, 30·0; H, 3·9; S, 11·7; Cl, 37·9. Calc. for $C_3H_3O_2SCl_2$: C, 29·6; H, 3·9; S, 15·8; Cl, 34·9%). The infrared absorption spectrum had many features in common with that of bis-2-chloroethyl carbonate;

however, two additional strong bands appeared at ~1150 and ~705 cm.$^{-1}$ which are tentatively assigned to C=S and C–S respectively. A C=O band appeared at 1732 cm.$^{-1}$ with a strong shoulder at 1741 cm.$^{-1}$ and a C–O band at 1270—1245 cm.$^{-1}$. In bis-2-chloroethyl carbonate these appeared at ~1755 cm.$^{-1}$ and 1280—1250 cm.$^{-1}$. Despite the poor agreement in the analytical data (several analyses were performed) this fraction appears to be substantially a mixture of the isomeric bis-2-chloroethyl thion- and thiol-carbonates.

Redistillation of the distillate that surged over during the initial distillation afforded ethylene dichloride, b. p. 83—83·5°, n_D^{20} 1·4444, and this must have originated from the decomposition of 2-chloroethyl chlorothioformate, initially formed.

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TEDDINGTON, MIDDLESEX. [*Received, February 25th*, 1957.]

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531. *Experiments on the Synthesis of the Pyrethrins. Part XIII.* Total Synthesis of* (±)-cis- *and* -trans-*Chrysanthemumdicarboxylic Acid,* (±)-cis- *and* -trans-*Pyrethric Acid, and Rethrins II.*

By L. CROMBIE, S. H. HARPER, and K. C. SLEEP.

(±)-*cis*- and -*trans*-Chrysanthemumdicarboxylic acids † are synthesised by treating *trans*-2 : 5-dimethylsorbic ester with diazoacetic ester. Their structures are established by ozonolysis to *meso*-*cis*- and (±)-*trans*-caronic acids respectively. The -*trans*-dicarboxylic acid is equated with the natural (+)-acid by infrared solution spectra. It follows that the natural acid has a *trans*-side-chain, and, from our previous work, can be correlated with glyceraldehyde.

Routes to 2 : 5-dimethylsorbic acid are investigated and a convenient synthesis from acetoacetaldehyde dimethylacetal is described. It is shown to be the *trans*-acid.

Dimethyl (±)-*cis*-, (±)-*trans*-, and (+)-*trans*-chrysanthemumdicarboxylate are converted into pyrethric acids by partial hydrolysis, and the structure of the (+)-*trans*-compound established by oxidative degradation and biological evidence. Esterification of allylrethrolone with pyrethric acids leads to the first totally synthetic rethrins II.

HYDROLYSIS of pyrethrin II (Ia) and cinerin II (Ib), which occur in natural pyrethrum extract, gives a substituted *cyclo*propane, chrysanthemumdicarboxylic acid (II; R = R′ = H). Staudinger and Ruzicka [1] established its structure as (+)-*trans*-3-(2-carboxyprop-1-enyl)-2 : 2-dimethyl*cyclo*propane-1-carboxylic acid by ozonising it to (−)-*trans*-caronic acid and pyruvic acid. On controlled alkaline hydrolysis of a crude semicarbazone they isolated the half methyl ester of chrysanthemumdicarboxylic acid (pyrethric acid) (II; R = H, R′ = Me) from which methyl pyruvate was obtained on ozonolysis. This

* Part XII, *J.*, 1957, 1083.

† As all the compounds mentioned in this paper have *trans*-side-chains, the prefix *cis* or *trans* used with chrysanthemumdicarboxylic acid and related substances refers only to the configuration about the *cyclo*propane ring. If differentiation is needed, *trans*$_c$- may be used to indicate the arrangement of the ring substituents and *trans*$_o$ to indicate the stereochemistry of the olefinic linkage, *e.g.*, (III; R = R′ = H) is *trans*$_o$: *cis*$_c$-chrysanthemumdicarboxylic acid.

[1] Staudinger and Ruzicka, *Helv. Chim. Acta*, 1924, **7**, 201.

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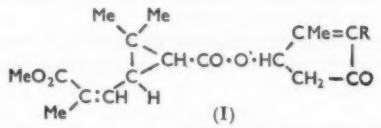
established that it is the acidic function attached to the *cyclo*propane ring which is involved in ester formation with the rethrolone fragment. Staudinger and Ruzicka's work left two stereochemical points unsettled: first, the configurative correlation with (+)-glyceraldehyde and, secondly, the stereochemistry of the side-chain double bond. Crombie and

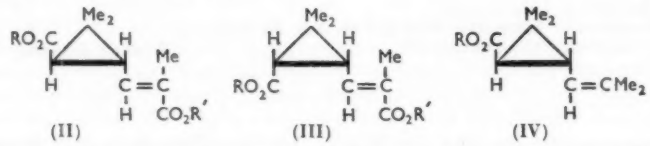


(I)

(Ia): R = $CH_2 \cdot CH{=}^{c}CH \cdot CH{=}CH_2$

(Ib): R = $CH_2 \cdot CH{=}^{c}CHMe$

Harper [2] established the configurative correlation for (+)-*trans*-chrysanthemic acid (IV), which also gives (−)-*trans*-caronic acid on ozonolysis, and it follows that the same relation must hold for (+)-*trans*-pyrethric acid and its rethrins II (cf. footnote on p. 2747). The structures are represented spatially in (II)—(IV). The stereochemistry of the side-chain double bond is clarified below.



(II) (III) (IV)

This paper is concerned with the synthesis of the chrysanthemumdicarboxylic acids, and a summary has appeared elsewhere.[3] Experiments on model compounds indicated that diazoacetic ester attacks the 4 : 5-double bond in sorbic and 2-methylsorbic ester, though yields are low, and, because of the number of stereoisomers possible, it is difficult to isolate crystalline products.[4] From the addition of diazoacetic ester to 2 : 5-dimethylsorbic ester only two geometrical arrangements of the substituents on the *cyclo*propane ring are possible, (II) and (III), and this route was pursued.

2 : 5-Dimethylsorbic acid had not previously been described and various preparations were investigated. Reformatski reaction between *iso*valeraldehyde and ethyl α-bromopropionate gave the expected ethyl 3-hydroxy-2 : 5-dimethylhexanoate, which resisted dehydration with phosphorus oxychloride, potassium hydrogen sulphate, or thionyl chloride in pyridine, but was dehydrated by phosphoric oxide. The product showed no high-intensity absorption between 215 and 300 mμ and only a weak double-bond stretching vibration, suggesting that it is (V) and not (VI). Dehydrogenation with *N*-bromo-

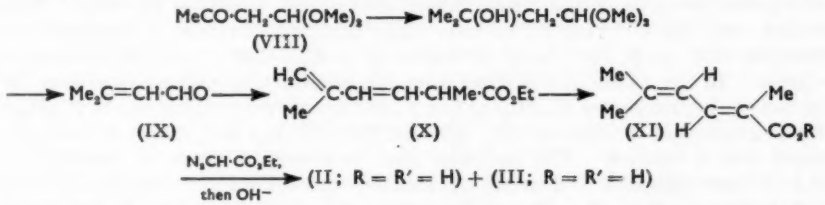
(V) $Me_2CH \cdot CH{:}CH \cdot CHMe \cdot CO_2Et$ $Me_2CH \cdot CH_2 \cdot CH{:}CMe \cdot CO_2Et$ (VI)

succinimide and pyridine gave a mixture having maxima at 225—227 and 269—276 mμ which probably contained ethyl 2 : 5-dimethylhexa-3 : 5- and -2 : 4-dienoate. When this was treated with phosphorus oxychloride (see below) and then hydrolysed, low yields of 2 : 5-dimethylsorbic acid were obtained. This result parallels the experience of Reid and Sause [5] who obtained only poor yields of 5-methylsorbic acid from a similar dehydrogenation procedure. As an alternative route, 1-bromo-3-methylbut-2-ene was converted into 2 : 5-dimethylhex-4-enoic acid by methylmalonic ester synthesis. The acid obtained from the decarboxylation step was contaminated with lactone produced by self-addition (cf. 5-methylhex-4-enoic acid, which, prepared by similar route,[6] is contaminated with 12% of lactone), and was freed from this, and esterified. Dehydrogenation with *N*-bromosuccinimide and pyridine gave discouraging results and the method was abandoned.

An obvious route to 2 : 5-dimethylsorbic acid is the Reformatski reaction between

[2] Crombie and Harper, *J.*, 1954, 470.
[3] Harper, Sleep, and Crombie, *Chem. and Ind.*, 1954, 1538.
[4] Harper and Reed, *J.*, 1955, 779.
[5] Reid and Sause, *J.*, 1954, 516.
[6] Linstead and Rydon, *J.*, 1933, 580.

β-methylcrotonaldehyde and α-bromopropionic ester but the relative inaccessibility of the aldehyde seemed a source of difficulty. Although a number of preparations are described,[7] none seemed suitable and we adapted a procedure for α-unsaturated aldehydes described by Price and Pappalardo.[8] These authors used acylacetaldehyde acetals prepared from chlorovinyl ketones, but Franke *et al.*[9] have made acetoacetaldehyde dimethyl acetal (VIII) readily available from diacetylene, and we used material from this source. This acetal with methylmagnesium bromide gave β-hydroxy*iso*valeraldehyde dimethyl acetal in 60% yield. Distillation with oxalic acid then gave β-methylcrotonaldehyde in 35—37% yield. A restriction on the method is that yields decline when the scale of the last step is above 0·3 mol. Fresh β-methylcrotonaldehyde was treated with activated zinc and ethyl α-bromopropionate under the usual Reformatski conditions, and, since the product was expected to be the hydroxy-ester, it was treated with phosphorus oxychloride. This procedure gave the expected ethyl 2 : 5-dimethylsorbate but treatment with phosphorus oxychloride has other significance and this is dealt with later.



Hydrolysis of ethyl 2 : 5-dimethylsorbate gave the crystalline acid, ultraviolet max. 274 mμ (ε 22,700), which absorbed two mols. of hydrogen over a platinum catalyst. Though the mother-liquors were searched, only one form, m. p. 137°, could be isolated. The resistance of 2 : 5-dimethylsorbic acid to cyclisation by mineral acid strongly supports the *trans*-configuration, for 5-methylhex-4-enoic acid is lactonised extremely easily under these conditions [6] and, structurally, *cis*-2 : 5-dimethylsorbic acid is still more favourably disposed for cyclisation. Esterification with diazomethane gave pure methyl *trans*-2 : 5-dimethylsorbate.

Addition of ethyl diazoacetate to ethyl 2 : 5-dimethylsorbate at 110—115° in the presence of copper bronze gave an ester $C_{14}H_{22}O_4$ in 41% yield, together with substantial amounts of unchanged sorbate. When hydrolysed, the new ester gave a mixture of two acids, the less soluble of which was isolated pure by crystallisation from dilute acetic acid. On ozonolysis it yielded (±)-*trans*-caronic acid and pyruvic acid (2 : 4-dinitrophenylhydrazone), showing that addition had occurred at the 4 : 5-double bond. On the reasonable assumption that the configuration of the 2 : 3-double bond is unaltered by the reaction, the less soluble acid is (±)-*trans*-3-(2-carboxyprop-*trans*-1-enyl)-2 : 2-dimethyl-*cyclo*propane-1-carboxylic acid (II; R = R′ = H). Its light absorption (max. 235—236 mμ; ε 14,900) agreed with that of natural (+)-chrysanthemumdicarboxylic acid (max. 235—236 mμ; ε 14,200). The synthetic acid was converted into the crystalline dimethyl ester and its infrared spectrum (in carbon tetrachloride solution) compared with that of natural dimethyl (+)-chrysanthemumdicarboxylate. The two spectra were identical (for the full curves see our note [3]) : the ultraviolet absorption was also identical within experimental error. Staudinger and Ruzicka's structure [1] is thus confirmed synthetically, and the side-chain configuration shown to be *trans*.

[7] *Inter al.*, Fischer, Ertel, and Löwenberg, *Ber.*, 1931, **64**, 30; Fischer and Löwenberg, *Annalen*, 1932, **494**, 263; Burkhardt, Heilbron, and Aldersley, B.P. 512,465; Jones and Weedon, *J.*, 1946, 937; Young and Linden, *J. Amer. Chem. Soc.*, 1947, **69**, 2912; Wendler and Slates, *ibid.*, 1950, **72**, 5341; Inouye and Shinohara, *Botyu-Kagaku*, 1954, **19**, 102; Julia and Surzur, *Compt. rend.*, 1954, **238**, 2426; Braude and Evans, *J.*, 1955, 3334.

[8] Price and Pappalardo, *J. Amer. Chem. Soc.*, 1950, **72**, 2613.

[9] Franke, Kraft, Tietjen, and Weber, *Chem. Ber.*, 1953, **86**, 793; Franke and Kraft, *Angew. Chem.*, 1955, **67**, 395.

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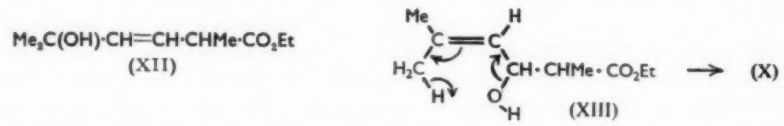
The mixed acids from hydrolysis of the diazoacetic ester reaction product were converted into their dimethyl esters to facilitate separation of the second acid. Crystalline dimethyl (±)-*trans*-chrysanthemumdicarboxylate was removed from a liquid ester, and the latter distilled. The crystalline and the liquid ester were isomeric and both absorbed at 235 mμ. The infrared spectrum of the liquid ester was different from that of dimethyl (+)chrysanthemumdicarboxylate (liquid films) especially between 1030 and 715 cm.$^{-1}$ and on hydrolysis gave a dibasic acid, m. p. 208—210°, which depressed the melting point of (±)-*trans*-chrysanthemumdicarboxylic acid (m. p. 207—208°). When ozonised, the liquid ester gave *meso-cis*-caronic acid so it must be methyl (±)-*cis*-3-(2-methoxycarbonylprop-*trans*-1-enyl)-2 : 2-dimethyl*cyclo*propane-1-carboxylate, and the acid (±)-*cis*-chrysanthemumdicarboxylic acid (III; R = R′ = H).

We now return to the Reformatski reaction between β-methylcrotonaldehyde and ethyl α-bromopropionate. If, from this reaction, ethyl 3-hydroxy-2 : 5-dimethylhex-4-enoate were isolated, and reaction with ethyl diazoacetate carried out, followed by dehydration, an alternative route to chrysanthemumdicarboxylic acid would be available. Inouye, Shinohara, and Ohno [10] claimed to have done this and obtained a chrysanthemumdicarboxylic acid, m. p. 180° (later revised to m. p. 185—186°): no spectroscopic data were given. In our hands, the product from the Reformatski reaction was, after distillation, not the hydroxy-ester ($C_{10}H_{18}O_3$) but a mixture of two isomeric esters ($C_{10}H_{16}O_2$). All the fractions had maxima at 227—228 and 276—277 mμ and absorbed two mols. of hydrogen over a catalyst. This indicates that they were mixtures of the retro-diene ethyl 2 : 5-dimethylhexa-3 : 5-dienoate (X) and the expected product, ethyl 2 : 5-dimethylhexa-2 : 4-dienoate (XI; R = Et): extinction data show that the lower-boiling fractions contained > 90% of the former and the higher-boiling ones about equal amounts of the two components. Infrared absorption confirmed the presence of a substance containing the groupings RR′C=CH$_2$ (888 cm.$^{-1}$), and R·CH=CHR′ (968 cm.$^{-1}$) in the low-boiling material, and the position of the ester-carbonyl absorption (1736 cm.$^{-1}$) indicated that it was α-saturated. When treated with phosphorus oxychloride, the ester (X) was readily isomerised into (XI). The formation of ethyl 2 : 5-dimethylhexa-3 : 5-dienoate by dehydration of the hydroxy-ester (XIII) might be due to prior anionotropic rearrangement followed by dehydration of the tertiary alcohol (XII), or to a cyclic concerted process as indicated.

Addition of ethyl diazoacetate to mixtures of ethyl 2 : 5-dimethylhexa-2 : 4- and -3 : 5-dienoate (containing mostly the latter) gave a product $C_{14}H_{22}O_4$. This was not a stereoisomer of diethyl chrysanthemumdicarboxylate for it showed no maximum above 210 mμ (ε 17,800 at 210 mμ) and absorbed 1·2 mols. of hydrogen on hydrogenation. The latter figure suggests that either the ester is a mixture or else it contains a grouping which is partially cleaved by hydrogenation. The ester was stable to phosphorus oxychloride and



on alkaline hydrolysis gave, in low yield, an acid, of m. p. 187° which was identical (mixed m. p.) with the substance originally claimed by Inouye and his co-workers [10] to be chrysanthemumdicarboxylic acid. The acid absorbed 2 mols. of hydrogen and had an ultraviolet maximum at 274 mμ, indicating the chromophore R·CMe:CH·CH:CMe·CO$_2$H. Infrared evidence is in agreement.

After publication of our note,[3] Inouye, Takeshita, and Ohno [11] confirmed our synthesis

[10] Inouye, Shinohara, and Ohno, *Botyu-Kagaku*, 1954, **19**, 35.
[11] Inouye, Takeshita, and Ohno, *ibid.*, 1955, **20**, 102; *Bull. Inst. Chem. Res. Kyoto Univ.*, 1955, **33**, 73.

of (±)-chrysanthemumdicarboxylic acid and now agree that the acid of m. p. 187° is not a stereoisomer of that system but a substituted sorbic acid. They claim to have obtained the latter by adding ethyl diazoacetate to ethyl 3-hydroxy-2 : 5-dimethylhex-4-enoate but this was not analysed and light absorption data, which would indicate that it had not dehydrated, appear to have been omitted. The acid of m. p. 187° is now formulated by them as (XIV) but it is difficult to explain its formation from our retrodiene (X). Our diene ester precursor cannot, on light-absorption grounds, be merely the ester derived from this acid. Since the acid gives lævulic acid on ozonolysis, structure (XV) is a reasonable

alternative. A speculative mode of formation is by attack of ethyl diazoacetate at the 5 : 6-double bond of (X) with the formation of an olefinic rather than a *cyclo*propane linkage (analogies for this exist [12]). Alkaline isomerisation of the intermediate unconjugated diene could then give the acid (XV) by prototropic shifts.[13] The by-product, and its origin, are being examined more closely.

In order to make totally synthetic rethrins II it was necessary to devise a procedure for preparing (±)-*trans*-pyrethric acid (II; R = H, R′ = Me). As the side-chain methoxycarbonyl group is tertiary and α-unsaturated, whereas the ring methoxycarbonyl group is secondary, it seemed possible that half-hydrolysis of the dimethyl ester might be successful. The procedure was tested on natural dimethyl (+)-*trans*-chrysanthemumdicarboxylate, and, when distilled, the product had $[\alpha]_D^{16}$ +103·4°, in good agreement with Staudinger and Ruzicka's value [1] of $[\alpha]_D^{18}$ +103·9° for natural pyrethric acid.* Confirmation of its structure was obtained by ozonising it to methyl pyruvate, and, when esterified with allylrethrolone, it gave a partially synthetic rethrin II with high insecticidal activity. The procedure was then applied to the preparation of totally synthetic (±)-*trans*-pyrethric acid: its infrared spectrum (liquid film) was identical with that of natural (+)-*trans*-pyrethric acid. If the partial hydrolysis was carried out in ethanol, the ethyl (±)-*trans*-half ester, resulting from ester interchange, could be isolated as a crystalline solid. (±)-*cis*-Pyrethric acid was also prepared. The pyrethric acids were converted into their acid chlorides and then esterified with (±)-allyl-rethrolones to give the first totally synthetic rethrins II. Biological data are summarised in the experimental section and it is material that (±)-allylrethronyl (+)-*trans*-chrysanthemate is 4·1 times as toxic as the (+)-*trans*-pyrethrate made by the partial hydrolysis procedure, for LaForge and his co-workers [14] found a ratio of 4·4 using (±)-allylrethronyl (+)-*trans*-pyrethrate prepared from natural pyrethric acid.

Natural (+)-*trans*-pyrethric acid has previously been re-esterified with natural (+)-*cis*-cinerolone and (+)-*cis*-pyrethrolone to give cinerin II and pyrethrin II. Since we have previously synthesised (±)-*cis*-cinerolone [15] and (±)-*cis*-pyrethrolone,[16] the problem of making the natural rethrins-II with the correct geometrical form at the two olefinic and the *cyclo*propane centres is now solved. Attention may be directed to improvements in

* This completes a total synthesis of natural (+)-pyrethric acid for Matsui, Miyano, and Yamashita (*Proc. Japan. Acad.*, 1956, **32**, 353) find that natural (+)-chrysanthemic acid (first synthesised by Campbell and Harper, *J.*, 1945, 283) can be converted into (+)-chrysanthemumdicarboxylic acid by oxidation with selenium dioxide, followed by treatment with silver oxide.

[12] von Auwers and Ungemach, *Ber.*, 1933, **66**, 1198; D'yakonov, *Zhur. obshchei Khim.*, 1949, **19**, 1891.

[13] Goldberg and Linstead, *J.*, 1928, 2343.

[14] LaForge, Gersdorff, Green, and Schechter, *J. Org. Chem.*, 1952, **17**, 381.

[15] Crombie and Harper, *Nature*, 1949, **164**, 534; *J.*, 1950, 1152; Crombie, Harper, Stedman, and Thompson, *J.*, 1951, 2445.

[16] Crombie, Harper, and Newman, *Chem. and Ind.*, 1954, 1109; *J.*, 1956, 3963.

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the synthetic methods and optical resolution of *cis*-pyrethrolone and *trans*-pyrethric acid. Information on the latter aspect has recently appeared.[17]

Experimental

Ultraviolet measurements were made in ethanol with a Unicam SP.500 instrument, and infrared measurements with Grubb-Parsons single- and double-beam spectrometers (rock-salt optics).

β-*Hydroxyisovaleraldehyde Dimethyl Acetal*.—Acetoacetaldehyde dimethyl acetal (132 g., 1 mole; b. p. 67—68°/15 mm., n_D^{20} 1·4138) was added slowly to a Grignard reagent prepared from magnesium (34 g., 1·4 g.-atoms) and methyl bromide in dry ether (400 ml.), at 20°. When reaction was complete, ammonium acetate solution was cautiously added, and the ethereal layer separated. The aqueous phase was extracted with ether (2 × 100 ml.), and the united ethereal solutions were dried ($MgSO_4$), evaporated, and distilled. After elimination of a fore-run, b. p. to 72°/14 mm., n_D^{20} 1·4228 (12·6 g.), β-hydroxy*iso*valeraldehyde dimethyl acetal (89 g., 60%), b. p. 72—79°/14 mm., n_D^{20} 1·4196, was obtained. A total of 850 g. of material was prepared (n_D^{20} 1·4190—1·4196), in yields varying from 48 to 60%.

β-*Methylcrotonaldehyde*.—β-Hydroxy*iso*valeraldehyde (39·7 g.), anhydrous oxalic acid (7·5 g.; prepared by azeotropic distillation with carbon tetrachloride), and quinol (0·5 g.) were distilled together at 10 mm., the still-head temperature being kept below 50° and the receiver at −30°. The distillate was fractionated to give, after removal of the methanol, β-methylcrotonaldehyde (8·3 g., 37%), b. p. 40—46°/13 mm., n_D^{20} 1·4550. The 2 : 4-dinitrophenylhydrazone had m. p. 184—185° (lit.,[7] b. p. 68—72°/95 mm.; 2 : 4-dinitrophenylhydrazone, m. p. 184—185°). Each batch was used immediately in the Reformatski reaction below. When the scale of the reaction was increased, yields diminished. A modification in which the acetal (44 g.) was added dropwise to anhydrous oxalic acid (8 g.) and quinol (0·8 g.) contained in a 50 ml. Claisen flask at 85—90°/2 mm. gave 35 g. of crude product. On redistillation through a short column, this yielded β-methylcrotonaldehyde (8·8 g., 35%), but the material was less pure than that from the first method (b. p. 44—60°/17 mm., n_D^{20} 1·4520).

Ethyl 2 : 5-*Dimethylhexa*-2 : 5-*dienoate* (2 : 5-*Dimethylsorbate*).—A few ml. of a mixture of β-methylcrotonaldehyde (11·0 g.), ethyl α-bromopropionate (25 g.), and dry benzene (30 ml.) was added to zinc wool (8·5 g.; activated by immersion in 2N-hydrochloric acid for 20 sec., followed by washing with water, acetone and ether, and drying under a vacuum) and dry benzene (10 ml.) containing a crystal of iodine. Reaction commenced, with vigorous refluxing, after warming and stirring, and the remainder of the aldehyde mixture was added dropwise so as to maintain steady refluxing. The product was heated on a water-bath for 2 hr., cooled, and stirred with ice-cold 2N-sulphuric acid (100 ml.). The benzene layer was isolated and washed with 10% sodium hydrogen carbonate solution, N-sulphuric acid (25 ml.), and water (2 × 25 ml.). The acidic washing was added to the 2N-acid used for decomposition and extracted with ether (2 × 25 ml.): these extracts were added to the benzene solution, the whole was dried, and the ether evaporated. Phosphorus oxychloride (8 g.) was added to the benzene solution, and the mixture heated under reflux for 20 min. The product was washed with water (2 × 50 ml.), then dried ($MgSO_4$), and the benzene distilled. Distillation of the residue yielded ethyl 2 : 5-dimethylsorbate (12·5 g., 57%), b. p. 112—114°/22 mm., n_D^{20} 1·5029. Light absorption: max. 276—277 mμ (ε 24,400). Replacement of benzene as solvent by tetrahydrofuran gave similar yields, but the working up was less convenient.

2 : 5-*Dimethylsorbic Acid*.—Ethyl 2 : 5-dimethylsorbate (9·3 g.) was heated under reflux with potassium hydroxide (9·3 g.) in ethanol (100 ml.) for 1 hr. The ethanol was distilled, water (50 ml.) added, and the product acidified to Congo-red. The precipitated 2 : 5-*dimethylsorbic acid* (6·4 g., 83%) had m. p. 132—134°. It was recrystallised from light petroleum (b. p. 80—100°) to m. p. 137° (5·5 g., 71%) and formed colourless needles (Found: C, 68·5; H, 8·5. $C_8H_{12}O_2$ requires C, 68·5; H, 8·6%). Light absorption: max. 274 mμ (ε 22,700). The infrared spectrum showed bands at 1677 (unsatd. CO_2H) and 1630 and 1597 cm.$^{-1}$ (conj. diene). When it was hydrogenated in ethyl acetate with Adams catalyst 1·98 mols. of hydrogen were absorbed. Its methyl ester, prepared by use of diazomethane, had b. p. 100—102°/14 mm., n_D^{20} 1·5167 (yield 87%), absorption max. 276 mμ (ε 24,200).

[17] Inouye and Ohno, *Bull. Inst. Chem. Res. Kyoto Univ.*, 1956, **34**, 90.

2 : 5-Dimethylsorbic acid (27 mg.) was heated under reflux for 40 min. with 2N-sulphuric acid. The acid was somewhat volatile in steam. After being set aside overnight, the solution was thoroughly extracted with ether, and the extracts were dried and evaporated. The infrared spectrum of the crude solid product (Nujol mull) was identical with that of 2 : 5-dimethylsorbic acid, and no lactone band was present.

Ethyl 2 : 5-*Dimethylhexa*-3 : 5-*dienoate*.—A Reformatski reaction was carried out as above with zinc wool (7·5 g.), β-methylcrotonaldehyde (8·5 g.), ethyl α-bromopropionate (21 g.), and dry tetrahydrofuran (40 ml.). Phosphorus oxychloride treatment was omitted and the *product*, when distilled at 0·2 mm., was separated into five fractions: (i) b. p. 52—53°, n_D^{20} 1·4587 (0·96 g.); (ii) b. p. 53—54°, n_D^{20} 1·4633 (3·99 g.); (iii) b. p. 54—59°, n_D^{20} 1·4655 (0·63 g.); (iv) b. p. 59—64°, n_D^{20} 1·4721 (1·63 g.); (v) b. p. 64—66°, n_D^{20} 1·4864 (3·70 g.) [Found, in fraction (ii) C, 71·2; H, 9·7. In fraction (iv): C, 69·8; H, 9·7. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6. $C_{10}H_{18}O_2$ requires C, 64·5; H, 9·8%]. Light absorption of fraction (ii), max. 228—229 mμ (ε 18,500) and 275—276 mμ (ε 2400).

A similar reaction was carried out with benzene as solvent and two main fractions taken: (*a*) b. p. 64—66°/0·5 mm., n_D^{20} 1·4611; (*b*) b. p. 74—80°/0·5 mm., n_D^{20} 1·4829. Light absorptions: (*a*) max. 229 mμ (ε 16,400) and 276—277 mμ (ε 2300); (*b*) max. 228—229 mμ (ε 8700) and 276—277 mμ (ε 10,900). On hydrogenation over 5% palladium–charcoal in ethyl acetate, (*a*) absorbed 2·08, and (*b*) 2·07 mols. of hydrogen. It was necessary to add a little Adams catalyst to complete the hydrogenation of (*a*). The light absorption data show that (ii) and (*a*) contain less than 10% of ethyl 2 : 5-dimethylsorbate. The composition of successive fractions can easily be followed by their infrared spectra using, in particular, bands at 1736 (α-saturated ester), 1705 (α-unsaturated ester), 968 (*trans*-CH=CH) and 888 (CH_2=CRR′) cm.$^{-1}$.

Isomerisation of Ethyl 2 : 5-*Dimethylhexa*-3 : 5-*dienoate to Ethyl* 2 : 5-*Dimethylsorbate*.—Fraction (*a*) above (1·0 g.; n_D^{20} 1·4611) was heated under reflux with phosphorus oxychloride (0·35 g.) in benzene (7 ml.) for 25 min. The product was washed with water (2 × 5 ml.), dried, evaporated, and distilled to give ethyl 2 : 5-dimethylsorbate (0·60 g.), b. p. 109—111°/16 mm., n_D^{20} 1·5030. On hydrolysis this gave a good yield of 2 : 5-dimethylsorbic acid, m. p. 133—135°, which when recrystallised had m. p. 137°, undepressed on admixture with the specimen prepared as above.

Ethyl 3-*Hydroxy*-2 : 5-*dimethylhexanoate*.—A Reformatski reaction [18] was carried out as described above with *iso*valeraldehyde (20 g.), ethyl α-bromopropionate (45 g.), zinc wool (20 g.), and benzene (40 ml.), a benzene solution of the product being treated under reflux (20 min.) with phosphorus oxychloride (12 g.). Working up and distillation gave *ethyl* 3-*hydroxy*-2 : 5-*dimethylhexanoate* (13·7 g., 31%), b. p. 104—108°/8 mm., n_D^{20} 1·4304, no dehydration having occurred. On redistillation the product had b. p. 113—114°/15 mm., n_D^{20} 1·4305 (Found: C, 64·3; H, 10·8. $C_{10}H_{20}O_3$ requires C, 63·8; H, 10·7. $C_{10}H_{18}O_2$ requires C, 70·55; H, 10·65%). It did not decolorise bromine in carbon tetrachloride, could not be hydrogenated over Adams catalyst, and was transparent in the region 213—300 mμ but showed strong hydroxyl absorption at 3435 cm.$^{-1}$.

A Reformatski reaction in which the phosphorus oxychloride treatment was omitted gave the same product, b. p. 104—108°/8 mm., n_D^{20} 1·4305, in 57% yield.

Ethyl 2 : 5-*Dimethylhex*-3-*enoate*.—Ethyl 3-hydroxy-2 : 5-dimethylhexanoate (5·0 g.) and phosphoric oxide (3·0 g.) were distilled together at 12 mm. The crude distillate had b. p. 78—83°/12 mm., n_D^{20} 1·4289. The distillates from two such experiments were fractionated, to give *ethyl* 2 : 5-*dimethylhex*-3-*enoate* (5·2 g., 58%), b. p. 74—81°/11 mm., n_D^{20} 1·4272—1·4282. The main fraction had b. p. 76—78°/11 mm. (Found: C, 70·9; H, 10·5. $C_{10}H_{18}O_2$ requires C, 70·55; H, 10·65%). There was no high-intensity maximum in the region 215—300 mμ.

Dehydrogenation of Ethyl 2 : 5-*Dimethylhex*-3-*enoate*.—The ester (5 g.) was heated under reflux with carbon tetrachloride (35 ml.), *N*-bromosuccinimide (5·4 g.), and a trace of benzoyl peroxide. Reaction began after 15 min. and the product was then heated for 45 min. more and finally cooled to 0°. The succinimide was filtered off and dry pyridine (3·63 g.) added to the filtrate. The mixture was heated under reflux (1 hr.), cooled, washed with 2N-hydrochloric acid and then water, and dried ($MgSO_4$). Removal of the solvent and distillation at 8 mm. gave fractions: (i) b. p. to 88°, n_D^{20} 1·4586 (0·27 g.); (ii) b. p. 88—94°, n_D^{20} 1·4555 (0·62 g.); (iii) b. p. 94—100°, n_D^{20} 1·4602 (0·76 g.); (iv) b. p. 100—108° n_D^{20} 1·4700 (1·06 g.). Fraction (ii)

[18] Raichstein, *J. Russ. Phys. Chem. Soc.*, 1907, **39**, 587.

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had max. 225 mμ (ε 11,500) and 269 mμ (ε 2600), and (iv) had max. 227 mμ (ε 9150) and 275—276 mμ (ε 4000).

Fraction (iv) (0·9 g.) was heated under reflux with phosphorus oxychloride (0·4 g.) in benzene (5 ml.) for 30 min. After washing with water, drying, and distillation, an ester (0·65 g.) was obtained having b. p. 99—103°/6 mm., n_D^{20} 1·4886. On hydrolysis this gave 2 : 5-dimethylsorbic acid (0·3 g.), m. p. 132—135°, raised on crystallisation to 137° (m. p. and mixed m. p.). Fraction (ii) (0·5 g.) on similar treatment gave 2 : 5-dimethylsorbic acid (0·07 g.), m. p. 137°. Fraction (iii) (0·6 g.) when hydrolysed without prior treatment with phosphorus oxychloride gave 2 : 5-dimethylsorbic acid (0·1 g.), m. p. 124—128°, raised by two recrystallisations to 137°.

1-Bromo-3-methylbut-2-ene.—3-Hydroxy-3-methylbut-1-ene was prepared by Campbell and Eby's method [19] in 34% yield and had b. p. 96·5—100·5°, n_D^{20} 1·4150. A mixture of the alcohol (12·5 g.) and dry pyridine (2·0 g.) was added slowly to a stirred solution of phosphorus tribromide (15 g.) in light petroleum (70 ml.; b. p. 40—60°), at 0°. After 30 min., ice-water was added and the petroleum layer separated and washed with sodium hydrogen carbonate solution and then water. Drying, evaporation, and distillation gave the bromide (8·25 g., 38%), b. p. 64—68°/70 mm., n_D^{20} 1·4958. By using the hydrobromic acid procedure of Mulliken *et al.* [20] the bromide was isolated in 28% yield, with b. p. 72—76°/80 mm., n_D^{20} 1·4934.

Diethyl 5-Methylhex-4-ene-2 : 2-dicarboxylate.—1-Bromo-3-methylbut-2-ene (21·1 g.) was added dropwise to ethyl sodiomethylmalonate prepared from sodium (3·3 g.) and ethyl methylmalonate (24·7 g.) in ethanol (80 ml.), and the product was heated under reflux for 2 hr. The ethanol was distilled and water (65 ml.) added to the residue. Separation of the organic layer, drying, evaporation, and distillation gave diethyl 5-methylhex-4-ene-2 : 2-dicarboxylate (19·5 g., 57%), b. p. 132—135°/16 mm., n_D^{20} 1·4410 (Found: C, 63·9; H, 8·8. Calc. for $C_{13}H_{22}O_4$: C, 64·4; H, 9·15%). Staudinger *et al.*[21] give b. p. 120—128°/12 mm.

2 : 5-Dimethylhex-4-enoic Acid.—The above ester (19·0 g.) was heated under reflux for 2 hr. with potassium hydroxide (13·2 g.) in ethanol (100 ml.). The ethanol was evaporated and water (60 ml.) added. After extraction with ether (4 × 15 ml.) the aqueous solution was acidified to Congo-red, and the product collected with ether. Evaporation gave the crude substituted malonic acid (14·5 g.), m. p. 86—89°. The latter (3·5 g.) was heated at 150° for 90 min. and extracted with 10% sodium hydrogen carbonate solution (50 ml.). The alkaline extract was thoroughly extracted with ether and then covered with a layer of ether and acidified at 0°, with vigorous shaking, by a solution of concentrated hydrochloric acid (6·3 ml.) in water (7 ml.). The ethereal layer was separated, washed, dried, and distilled, to give 2 : 5-*dimethylhex-4-enoic acid* (0·9 g., 34%), b. p. 100—103°/0·7 mm., n_D^{20} 1·4490 (Found: C, 66·9; H, 9·7%; equiv., 143·6. $C_8H_{14}O_2$ requires C, 67·55; H, 9·9%; equiv., 142).

The product from direct decarboxylation was contaminated with lactone: in one experiment the purification was omitted. On distillation two fractions were taken: (i) b. p. 125—127°/17 mm., n_D^{20} 1·4483 (18%), and (ii) b. p. 127—130°/17 mm., n_D^{20} 1·4496 (48%). The equivalent of (ii) was 205 (equivs. were determined with cold ethanolic alkali).

2 : 5-Dimethylhex-4-enoic acid was converted into its methyl ester with diazomethane and this had b. p. 78—80°/16 mm., n_D^{20} 1·4334. Bromination with *N*-bromosuccinimide, followed by dehydrobromination with pyridine or triethylamine, gave unpromising mixtures.

Stereoisomeric (±)-Diethyl Chrysanthemumdicarboxylates.—Ethyl 2 : 5-dimethylsorbate (11·0 g.), light petroleum (25 ml., b. p. 100—120°), and copper bronze (0·5 g.) [22] were heated to 100°. Ethyl diazoacetate (15 g.) was added slowly: there was vigorous evolution of nitrogen and the temperature in the flask rose to 115°. The product was heated under reflux for 2 hr., the copper bronze filtered off, and the filtrate distilled. After a fore-run, b. p. 42—98°/0·07 mm., n_D^{20} 1·4671—1·4678 (6·3 g.), *diethyl chrysanthemumdicarboxylate* (6·78 g., 41%), b. p. 98—106°/0·07 mm., n_D^{20} 1·4706, was obtained. There was a large residue. The redistilled analytical specimen had n_D^{20} 1·4726 (Found: C, 65·8; H, 8·8. $C_{14}H_{22}O_4$ requires C, 66·1; H, 8·7%).

In another experiment, ethyl 2 : 5-dimethylsorbate (12·0 g.) and ethyl diazoacetate (8·5 g.) were allowed to react under the above conditions. This gave a fore-run (9·7 g.), b. p. 54—104°/0·4 mm., n_D^{20} 1·4885—1·4947, and diethyl chrysanthemumdicarboxylate (3·82 g.),

[19] Campbell and Eby, *J. Amer. Chem. Soc.*, 1941, **63**, 216, 2683.
[20] Mulliken, Wakeman, and Gerry, *ibid.*, 1935, **57**, 1605.
[21] Staudinger, Muntwyler, Ruzicka, and Seilt, *Helv. Chim. Acta*, 1924, **7**, 390.
[22] Loose, *J. prakt. Chem.*, 1909, **79**, 505.

b. p. 104—118°/0·4 mm., n_D^{20} 1·4748. When the fore-run (9·7 g.) was again treated with ethyl diazoacetate (6·6 g.), a further 2·88 g. of dicarboxylate (b. p. 109—120°/0·45 mm., n_D^{20} 1·4710), making a total yield of 33%, was obtained.

The fore-runs remaining from such experiments were united: they showed absorption at 276 mμ and on redistillation had n_D^{20} 1·4694—1·4775. The united fractions (23 g.) yielded 2 : 5-dimethylsorbic acid (7·6 g.), m. p. 137°, on hydrolysis.

Stereoisomeric Ethyl Methyl (±)-*Chrysanthemumdicarboxylates.*—Methyl 2 : 5-dimethylsorbate (13 g.) when treated with ethyl diazoacetate (19 g.) as above gave material, b. p. 54—98° (mainly 54°)/0·25 mm., n_D^{20} 1·5000, and then the stereoisomeric dicarboxylates (7·0 g., 35%), b. p. 98—105°/0·2 mm., n_D^{20} 1·4763. This fraction was hydrolysed to the mixed acids (5·12 g., 89%), m. p. 165—185° (see below for separation).

Hydrolysis of Diethyl (±)-*Chrysanthemumdicarboxylate.*—The ester (6·7 g.; n_D^{20} 1·4706) was heated under reflux with potassium hydroxide (6 g.) in ethanol (70 ml.) for 1 hr. and the ethanol then evaporated. Water (60 ml.) was added to the residue, and the solution extracted with ether (3 × 15 ml.). Ether remaining in the aqueous phase was removed *in vacuo* and the solution acidified. The oily solid which separated solidified overnight and was then filtered off (4·51 g.). Fractional crystallisation from 5% acetic acid gave pure (±)-trans-*chrysanthemumdicarboxylic acid* (0·73 g.), m. p. 206·5—208° (Found: C, 60·4; H, 7·3%; equiv., 99·6. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%; equiv., 99·1). Light absorption: max. 235—236 mμ (ε 14,900).

Ozonolysis of (±)-trans-*Chrysanthemumdicarboxylic Acid.*—Ozonised oxygen was passed through a suspension of the acid (0·29 g.) in chloroform (20 ml.) at 0° until all the solid dissolved and absorption of ozone was complete. The solvent was removed *in vacuo* at 20° and the ozonide warmed with water (15 ml.) for 15 min. The water was distilled and the distillate treated with 2 : 4-dinitrophenylhydrazine in dilute hydrochloric acid: a yellow derivative was formed and, twice crystallised from glacial acetic acid, gave pyruvic acid 2 : 4-dinitrophenylhydrazone (0·09 g.), m. p. and mixed m. p. 220—221°. The residue from the distillation slowly solidified and was twice crystallised from nitromethane, to give (±)-*trans*-caronic acid (0·11 g.), m. p. and mixed m. p. 218—220°.

Authentic (±)-*trans*-caronic acid was prepared by ozonising (±)-*trans*-chrysanthemic acid, and, crystallised from nitromethane, had m. p. 219—220°. Similarly, (±)-*cis*-chrysanthemic acid gave *meso-cis*-caronic acid, m. p. 179—180° (from nitromethane).

Dimethyl (±)- *and* (+)-trans-*Chrysanthemumdicarboxylate.*—The synthetic (±)-acid (0·4 g.) with diazomethane in ether gave the (±)-trans-*ester* (0·33 g., 66%), m. p. 77—78·5°, raised on crystallisation from light petroleum (b. p. 60—80°) to m. p. 80—80·5°. It formed colourless prisms (Found: C, 63·4; H, 7·9. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%). Light absorption: max. 236 mμ (ε 16,800).

Naturally derived chrysanthemumdicarboxylic acid, m. p. 167—170°, was similarly esterified and the ester distilled (b. p. 83—84°/0·07 mm., n_D^{20} 1·4818; 79%). Light absorption: max. 236 mμ (ε 16,200). Staudinger and Ruzicka [1] give b. p. 87—88°/0·25 mm.

The two esters, when compared as 15% solutions in carbon tetrachloride, had identical infrared spectra.

(±)-cis-*Chrysanthemumdicarboxylic Acid.*—Mixed chrysanthemumdicarboxylic acids (9·18 g., 85%), m. p. 150—185°, were obtained by hydrolysing the reaction product, diethyl chrysanthemumdicarboxylate (13·8 g., n_D^{20} 1·4704—1·4728), as described above. The acids with diazomethane gave a semisolid mixture of dimethyl esters (10·0 g., 95%). When crystallised from light petroleum (b. p. 60—80°) dimethyl (±)-*trans*-chrysanthemumdicarboxylate (4·1 g.) separated, having m. p. 77—80°. This was filtered off and the filtrate evaporated and distilled. Five fractions were taken, the main one having b. p. 93—94°/0·2 mm., n_D^{20} 1·4825 (2·59 g.). There was a further 1·15 g. of product, b. p. 89—96°/0·2 mm., n_D^{20} 1·4858—1·4831. Subsequent operations were carried out on the main fraction which was nearly pure dimethyl (±)-*cis*-chrysanthemumdicarboxylate, max. 235 mμ (ε 12,800).

The ester (0·5 g.) was hydrolysed in the usual way to (±)-cis-*chrysanthemumdicarboxylic acid* (0·3 g.), m. p. 198—207°, raised by two crystallisations from nitromethane to 208—210° (Found: C, 60·6; H, 6·8%; equiv., 100·3. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%; equiv., 99·1). Light absorption: max. 235 mμ (ε 14,200). When this product was mixed with the (±)-*trans*-acid described above, the m. p. was 175—186°.

A similar separation was also carried out on the mixed acids (5·12 g.) obtained from the

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ethyl methyl chrysanthemumdicarboxylate product. These gave the dimethyl ester mixture (5·52 g., 94%) which yielded methyl (±)-*trans*-chrysanthemumdicarboxylate (2·6 g.), m. p. and mixed m. p. 80°, and the methyl (±)-*cis*-ester (1·43 g.), b. p. 102—104°/0·35 mm., n_D^{20} 1·4835. The infrared spectrum of the latter was identical with that of the specimen described above.

Ozonolysis of Dimethyl (±)-cis-*Chrysanthemumdicarboxylate.*—Excess of ozone was passed through a solution of the methyl ester (1·0 g.) in methylene chloride (25 ml.) at 0°. The solvent was removed *in vacuo* at 20° and a solution of glacial acetic acid (2 ml.) in water (15 ml.) added to the residue, followed by 30% hydrogen peroxide (2 ml.). The solution was heated under reflux (1 hr.), cooled, and extracted with ether (4 × 5 ml.). The ethereal solution was dried and the solvent evaporated, leaving a solid residue which when crystallised from nitromethane yielded *meso-cis*-caronic acid (0·20 g.), m. p. 166—172°, raised by two further crystallisations to m. p. 178—179° (and mixed m. p.).

Under identical conditions methyl (±)-*trans*-chrysanthemate yielded (±)-*trans*-caronic acid, m. p. and mixed m. p. 218—220°, and not the half methyl ester.

Addition of Ethyl Diazoacetate to Ethyl 2 : 5-*Dimethylhexa*-3 : 5-*dienoate.*—Fractions (i), (ii), and (iii) from the Reformatski reaction described on p. 2749 were united: they contained approx. 90% of ethyl 2 : 5-dimethylhexa-3 : 5-dienoate. The material (5·2 g.) was dissolved in light petroleum (15 ml.; b. p. 100—120°), and copper bronze (0·1 g.) added. Ethyl diazoacetate (3·0 g.) was added dropwise to the mixture at 110° and the reaction carried out and the product worked up in the usual way. Fractionation gave an ester (4·48 g.), b. p. 104—110°/0·4 mm., n_D^{20} 1·4609—1·4613. The analytical specimen had b. p. 106—108°/0·4 mm., n_D^{20} 1·4612 (Found: C, 66·1; H, 8·6. Calc. for $C_{14}H_{22}O_4$: C, 66·1; H, 8·7%). Microhydrogenation, 1·2H_2. Light absorption: no max. > 210 mμ: at 210 and 230 mμ, ε was 17,800 and 2,500 respectively: there was an inflexion at 219 mμ (ε 5800). Allan, Jones, and Whiting [23] give max. 204·5 mμ (ε 16,500) for methyl *trans*-crotonate. The ester showed infrared absorption at 1724 (α-unsaturated ester), 1640 (C=C), and 977 (*trans*-CH=CH·CO_2R?) cm.$^{-1}$. There was a strong band at 1176 cm.$^{-1}$.

A similar experiment with fractions (iv) and (v) (p. 2749) (5·0 g.) gave the same ester (3·16 g.), b. p. 94—99°/0·2 mm., n_D^{20} 1·4634—1·4639 (Found: C, 65·6; H, 8·8%). When heated under reflux (3·0 g.) with phosphorus oxychloride (1·7 g.) in benzene (14 ml.) for 20 min., the ester (2·0 g.) was recovered unchanged (b. p. 102—107°/0·25 mm., n_D^{20} 1·4629—1·4639).

The Conjugated Diene Acid, m. p. 187°.—The ester (4·2 g.) obtained from the first experiment described immediately above gave crude acid (2·71 g.), m. p. 160—172°, on alkaline hydrolysis. Five crystallisations from nitromethane gave pure *acid* (0·90 g.), m. p. 187°. Ester (2·0 g.) from the second experiment above gave crude acid (1·19 g.), m. p. 144—158°, raised by six crystallisations to 187° (0·28 g.): it was identical with the first specimen (Found: C, 60·7; H, 7·0. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%). Light absorption: max. 272—275 mμ (ε 31,400). Another specimen had max. 274 mμ (ε 24,500). On hydrogenation in methanol with palladium–barium sulphate, 1·99 mols. of hydrogen were absorbed. The infrared spectrum showed bands at 1694 (α-unsaturated acid), 1626 and 1600 (conjugated diene) cm.$^{-1}$.

A suspension of the acid (0·45 g.) in methylene chloride (15 ml.) was ozonised at 0° and the ozonide decomposed with water (15 ml.). The product was distilled but the distillate gave no identifiable 2 : 4-dinitrophenylhydrazone. The residue after distillation gave lævulic acid 2 : 4-dinitrophenylhydrazone, m. p. 212—213° (0·05 g.), mixed m. p. with an authentic specimen (m. p. 213°), 210—212°.

(±)-trans-*Pyrethric Acid.*—Synthetic dimethyl (±)-*trans*-chrysanthemumdicarboxylate (2·9 g.), m. p. 80°, was dissolved in absolute methanol (35 ml.), 0·494N-methanolic potassium hydroxide (25·9 ml.) was added, and the solution set aside for 22 hr. It was then heated under reflux (75 min.) and the methanol evaporated *in vacuo*. Water (30 ml.) was added and the unchanged dimethyl chrysanthemumdicarboxylate (0·65 g., m. p. 77—80°) filtered off and washed with water. The filtrate was extracted with ether and acidified to Congo-red. The precipitated oil was collected with ether (5 × 10 ml.), and the ethereal solution washed with a little water and dried ($MgSO_4$). Evaporation and distillation of the residue (1·72 g.) gave (±)-trans-*pyrethric acid* (1·08 g.), b. p. 129—143°/0·06 mm., as a viscous liquid (Found: C, 62·1; H, 7·4%; equiv., 212. $C_{11}H_{16}O_4$ requires C, 62·25; H, 7·6%; equiv., 212). Light absorption: max. 235 mμ (ε 15,900). After more than a year, specimens of this, and of the (±)-*cis*-stereoisomer, had crystallised.

[23] Allan, Jones, and Whiting, *J.*, 1955, 1865.

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(+)-trans-*Pyrethric Acid.*—Dimethyl ester of naturally derived chrysanthemumdicarboxylic acid (4·64 g.), b. p. 105°/0·5 mm., was half-hydrolysed as above and the crude product distilled to give (+)-trans-*pyrethric acid* (2·77 g.), b. p. 130—145°/0·06 mm. (Found: C, 62·1; H, 7·6%; equiv., 210), absorption max. 236 mμ (ε 15,300), $[\alpha]_D^{16}$ +103·4° (*c* 1·18% in CCl_4). Staudinger and Ruzicka [1] give b. p. 129—130°/0·33 mm., $[\alpha]_D^{18}$ +103·9° (*c* 9·3% in CCl_4), for natural pyrethric acid.

Excess of ozone was passed through (+)-*trans*-pyrethric acid (0·6 g.) in methylene chloride (20 ml.) at 0°. The solvent was evaporated at 20° and water (25 ml.) added: the mixture was heated to 50° for 5 min. and poured into a solution of 2:4-dinitrophenylhydrazine in dilute hydrochloric acid. The precipitate (0·35 g.) was filtered off and dried. On treatment with benzene an insoluble yellow derivative remained undissolved, which when crystallised from light petroleum (b. p. 80—100°)–dioxan gave methyl pyruvate 2:4-dinitrophenylhydrazone (0·08 g.), m. p. 189—190°. After chromatography of the benzene solution on alumina, followed by elution with ether, the top orange band remaining on the column was isolated and extracted with sodium hydrogen carbonate solution. Acidification of the extract precipitated an acidic 2:4-dinitrophenylhydrazone (0·11 g.), m. p. 193—196°. When crystallised from dilute acetic acid small yellow needles, m. p. 198—199°, were obtained: the compound was not further identified but it may be the derivative of *trans*-3-formyl-2:2-dimethyl*cyclo*propane-1-carboxylic acid.

(±)-cis-*Pyrethric Acid.*—Dimethyl (±)-*cis*-chrysanthemumdicarboxylate (2·04 g.) was half-hydrolysed with 0·494N-methanolic potassium hydroxide (18·26 ml.) as above. The crude acid (0·76 g.) was distilled to give (±)-cis-*pyrethric acid* (0·44 g.), b. p. 130—147°/0·1 mm. (Found: C, 62·2; H, 7·5%; equiv., 206), absorption max. 233 mμ (ε 11,900).

(±)-trans-*Di- and Mono-ethyl Chrysanthemumdicarboxylate.*—Dimethyl (±)-*trans*-chrysanthemumdicarboxylate (3·0 g.) was half-hydrolysed with 0·488N-ethanolic potassium hydroxide (26·0 ml.) and worked up as previously described. The neutral product (0·77 g.) had m. p. 32·5—33·5° and analysed correctly for the *diethyl ester* (Found: C, 66·3; H, 8·5. $C_{14}H_{22}O_4$ requires C, 66·1; H, 8·7%). The acidic product, on distillation, gave *ethyl hydrogen* (±)-trans-*chrysanthemumdicarboxylate*, b. p. 135—143°/0·04 mm., m. p. 78° (Found: C, 63·7; H, 8·0%; equiv., 220, 222. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%; equiv., 226). Light absorption: max. 236 mμ (ε 16,100).

(±)-*Allylrethronyl* (±)-trans-*Pyrethrate.*—A solution of (±)-*trans*-pyrethric acid (0·69 g.) in light petroleum (7 ml.; b. p. 40—60°) containing thionyl chloride (0·43 g.) was set aside for 3 days. The light petroleum was evaporated and dry benzene (8 ml.) added. This solution was added to (±)-allylrethrolone (0·50 g.) and dry pyridine (0·51 g.) in dry benzene (5 ml.). Pyridine hydrochloride was at once precipitated and after 4 hr. the product was washed with saturated sodium hydrogen carbonate solution, dilute hydrochloric acid, and finally with water. The benzene solution was dried, evaporated, and distilled. After elimination of a small forerun, (±)-allylrethronyl (±)-*trans*-pyrethrate was collected (0·32 g.; b. p. 170—184°/0·04 mm.). The substance could not be completely purified by distillation on the scale used (Found: C, 67·8; H, 7·4. Calc. for $C_{20}H_{26}O_5$: C, 69·35; H, 7·6%). Light absorption: max. 235 mμ (ε 26,200).

(±)-*Allylrethronyl* (±)-cis-*Pyrethrate.*—This was prepared by the above method from (±)-*cis*-pyrethric acid (0·195 g.) and allylrethrolone (0·13 g.). The ester (0·181 g.) was not distilled but heated at 100°/0·02 mm. for 30 min. and then at 70° for 90 min. (Found: C, 67·8; H, 7·3%). Light absorption: max. 232—233 mμ (ε 22,800).

(±)-*Allylrethronyl* (+)-trans-*Pyrethrate.*—By the same procedure, (+)-*trans*-pyrethric acid (1·0 g.) was converted into (±)-*allylrethronyl* (+)-trans-*pyrethrate* (0·50 g.), b. p. 170—180°/0·02 mm. (Found: C, 69·3; H, 7·5%). Light absorption: max. 232—234 mμ (ε 27,300).

Biological Testing.—The rethrins prepared above were tested for insecticidal activity against houseflies with results summarised below. The potency is expressed relatively to a standard natural pyrethrum extract and is on a weight basis.

	Relative potency
(±)-Allylrethronyl (+)-*trans*-chrysanthemate	3·16
(±)- ,, (±)-*trans*- ,,	1·53
(±)- ,, (±)-*cis*- ,,	1·12
(±)- ,, (+)-*trans*-pyrethrate	0·77
(±)- ,, (±)-*trans*- ,,	0·45
(±)- ,, (±)-*cis*- ,,	0·41

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532. *Stereochemical Studies of Olefinic Compounds. Part VI.* Preparation of the Four Stereoisomeric Sorbyl Alcohols from a Single Precursor.*

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The four stereoisomeric hexa-2 : 4-dienols (sorbyl alcohols) are prepared from 4-toluene-*p*-sulphonyloxypent-1-yne. The latter is converted, by an elimination reaction and fractionation, into the known *cis*- and *trans*-pent-3-en-1-ynes. From these, hex-*cis*- and -*trans*-4-en-2-ynols are prepared. Partial catalytic hydrogenation gives hexa-*cis*-2 : *cis*-4- and -*cis*-2 : *trans*-4-dienol respectively, whilst reduction with lithium aluminium hydride gives hexa-*trans*-2 : *cis*-4- and -*trans*-2 : *trans*-4-dienol. The sorbyl alcohols are compared with specimens obtained by independent routes.

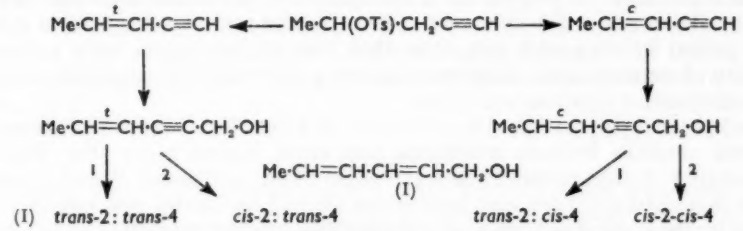
In recent work it has been possible to synthesise all four stereochemical forms of unsymmetrical conjugated dienes. The first examples reported [1] were the deca-2 : 4-dienoic acids, their methyl esters and other derivatives, and the deca-2 : 4-dienols. The latter were obtained from the methyl decadienoates by reduction with lithium aluminium hydride: it was shown that this reagent does not cause stereomutation. Soon after, Allan, Jones, and Whiting reported [2] that with their preparation of hexa-*trans*-2 : *cis*-4- and -*cis*-2 : *cis*-4-dienoic acid, the four stereoisomeric sorbic acids were known. The present work concerns the four sorbyl alcohols which were of interest in connexion with the stereoisomeric nona-5 : 7-dien-2-ones. Formally, they should be obtainable from the corresponding sorbic esters by reduction with lithium aluminium hydride, but we have used a single precursor for their preparation. During this work, Butenandt, Hecker, and Zachau [3] reported that they had made these substances by different means and their results are mentioned below. According to Butenandt *et al.*,[3,4] the sorbyl alcohols are of interest in connection with the sex-attractant substance of the silk-spinner.

The primary precursor used in our work was 4-toluene-*p*-sulphonyloxypent-1-yne which was converted into pent-3-en-1-yne by treatment with alkali.[5] Pent-3-en-1-yne obtained by this procedure is a mixture of *cis*- and *trans*-isomers [6] which were separated by distillation. The two hydrocarbons were converted into their Grignard reagents and the latter treated with formaldehyde to give *cis*- and *trans*-hex-4-en-2-ynol. Catalytic partial

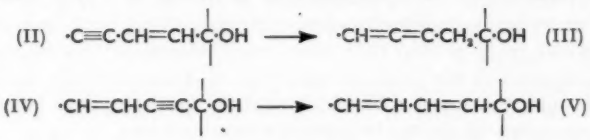
* Part V, *J.*, 1956, 136.

[1] Crombie, *J.*, 1955, 1007.
[2] Allan, Jones, and Whiting, *J.*, 1955, 1862.
[3] Butenandt, Hecker, and Zachau, *Chem. Ber.*, 1955, **88**, 1185.
[4] Butenandt, *Jahresber. preuss. Akad. Wiss.*, 1939, 97; *Naturwiss. Rdsch.*, 1955, **8**, 457.
[5] Eglinton and Whiting, *J.*, 1950, 3650.
[6] Allan and Whiting, *J.*, 1953, 3314; cf. Bruun, Christensen, Haug, Stene, and Sörensen, *Acta Chem. Scand.*, 1951, **5**, 1244.

hydrogenation of these alcohols, with quinoline-treated Lindlar catalyst [7] and absorption of 0·9 mol. of hydrogen, gave, after distillation, hexa-*cis*-2 : *cis*-4- and -*cis*-2 : *trans*-4-dienol which were characterised as crystalline α-naphthylurethanes. Light absorption data in Tables 1 and 2 relate to materials purified by distillation only, and not regenerated from recrystallised derivatives.



It has recently been shown [8] that treatment of an enyne system (II) with lithium aluminium hydride gives an allene (III) whereas the related enyne (IV) gives the conjugated diene (V). The behaviour of *cis*- and *trans*-hexenynol is in agreement, the former



giving hexa-*trans*-2 : *cis*-4-dienol and the latter hexa-*trans*-2 : *trans*-4-dienol. For data see Tables.

TABLE 1. *Data for the stereoisomeric hexa*-2 : 4-*dienols.*

Hexadienol	Source	$\lambda_{max.}$ (mμ)	ε	α-Naphthylurethane, m. p.	Hexadienol	Source	$\lambda_{max.}$ (mμ)	ε	α-Naphthylurethane, m. p.
trans-2 : *trans*-4	1	227	24,500	98—99°	*cis*-2 : *trans*-4 ...	1	229	19,800	96·5—97·5
	2	227	25,500	99·5—100		4	229	22,100	96—97
trans-2 : *cis*-4 ...	1	230	23,500	100—101	*cis*-2 : *cis*-4	1	230	14,700	88·5—89·5
	3	229·5	21,450	99—101		3	231	16,850	89—90

Sources: 1, From 4-toluene-*p*-sulphonyloxypent-1-yne. 2, From hexa-*trans*-2 : *trans*-4-dienoic ester. 3, Data given by Butenandt *et al.*[3]; see also Experimental section. 4, From hexa-*cis*-2 : *trans*-4-dienoic acid.

TABLE 2. *Comparison of infrared bands of stereoisomeric hexa- and deca*-2 : 4-*dienols* [1] *(films) and their tentative assignments.*

Dienol	$\nu C{=}C_I$	$\nu C{=}C_{II}$	Mean $\nu C{=}C$	$\Delta C{=}C$	$\delta'(CH{=}CH)_2$		
Hexa-*trans*-2 : *trans*-4	1661	1626 [a]	1644	35	1003i	987	— [b]
Deca-*trans*-2 : *trans*-4	1660	1626	1643	34	1008i	986	—
Hexa-*trans*-2 : *cis*-4	1653	161	1633	40	999	982	947
Deca-*trans*-2 : *cis*-4	1655 [c]	1616 [c]	1635	39	1003	983	948
Hexa-*cis*-2 : *trans*-4	1653	1613	1633	40	1001	986	952
Deca-*cis*-2 : *trans*-4	1652	1609	1630	43	997i	984	952
Hexa-*cis*-2 : *cis*-4	1647	1600	1624	47	—	— [d]	— [d]
Deca-*cis*-2 : *cis*-4	1651	1601	1626	50	—	— [d]	— [d]

[a] There is a similar band at 1605 cm.$^{-1}$ which is absent in deca-*trans*-2 : *trans*-4-dienol. [b] There is a band at 950 cm.$^{-1}$ which probably is not of stereochemical significance. [c] Other weak bands occur in this region. [d] Weak bands or inflexions in this region are neglected as they are likely to be due to impurity or other causes and are probably not of stereochemical significance.

[7] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.

[8] Chanley and Sobotka, *J. Amer. Chem. Soc.*, 1949, **71**, 4140; Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094; Bharucha and Weedon, *J.*, 1953, 1584; Bates, Jones, and Whiting, *J.*, 1954, 1854; Oroshnick, *J. Amer. Chem. Soc.*, 1955, **77**, 4048.

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To confirm the identity of the above specimens and estimate their purity, it was necessary to examine sorbyl alcohols from different sources. Hexa-*trans*-2 : *trans*-4-dienol is well known [9] and was prepared by reduction of ethyl *trans-trans*-sorbate with lithium aluminium hydride. Hexa-*cis*-2 : *trans*-4-dienol was made by similar reduction of hexa-*cis*-2 : *trans*-4-dienoic acid which is produced by treating δ-hexenolactone with sodium methoxide in methanol : [10] preparation of this hexadienol by a similar route has since been reported by Butenandt *et al.*[3] The *cis*-2 : *trans*-4 alcohol made by this method is rather purer, as judged by ultraviolet data, than that from the pentenyne route and reflects the inability of currently used catalysts to achieve a high degree of selectivity during the partial hydrogenation of enynes and diynes.

The independent preparation of hexa-*trans*-2 : *cis*-4-dienol was approached through the Reformatski reaction between but-2-ynal and ethyl bromoacetate. For large-scale preparation of 1 : 1-diethoxybut-2-yne a procedure based on Claisen's [11] and Viguier's [12] work was employed (cf. Lunt and Sondheimer [13]) and the acetal was converted into but-2-ynal by the method of Lunt *et al.* Reformatski reaction gave ethyl 3-hydroxyhex-4-ynoate which was dehydrated with phosphoric oxide to ethyl hex-*trans*-2-en-4-ynoate. Semihydrogenation of ethyl 3-hydroxyhex-4-ynoate gave ethyl 3-hydroxyhex-*cis*-4-enoate but, as experienced with an analogue of this acid,[1] no dehydration procedure could be found which did not cause complete or partial stereomutation of the *cis*-4-linkage. Partial hydrogenation of ethyl hex-*trans*-2-en-4-ynoate in the usual way gave ethyl hex-*trans*-2 : *cis*-4-enoate which was reduced to hexa-*trans*-2 : *cis*-4-dienol. The extinction coefficient of the latter (18,400) made it clear that some overhydrogenated material was present but work on the purification of this (and of hexa-*cis*-2 : *cis*-4-dienol which we had made from hexa-2 : 4-diynol and converted into the α-naphthylurethane) was discontinued when Butenandt's paper appeared giving the necessary reference data.

Butenandt *et al.* prepared hexa-*trans*-2 : *cis*-4-dienol by partial hydrogenation of hex-2-en-4-yn-1-ol and hexa-*cis*-2 : *cis*-4-dienol by similar treatment of hexa-2 : 4-diynol. As has been our experience,[1,14] the hydrogenation was incompletely selective and the alcohols were converted into crystalline 3-nitrophthalates, purified by Craig distribution and then regenerated. The regenerated alcohols were obtained only on a small scale (*e.g.*, 31 mg. of the *cis-cis*-alcohol) but provide a valuable reference for ultraviolet data. Table 1 indicates that, judged by this criterion, our hexa-*trans*-2 : *cis*-4-dienol was a little purer than Butenandt's even though it had only been purified by distillation, but the *cis-cis*-specimen was a little less pure. In each case the α-naphthylurethane of the hexadienol prepared from 4-toluene-*p*-sulphonyloxypent-1-yne did not depress the m. p. of the corresponding compound obtained by an independent route. In agreement with Butenandt *et al.*, we find that admixture of any pair of stereoisomeric α-naphthylurethanes causes a clear melting-point depression.

The data in Table 1 show the characteristic shift of $\lambda_{max.}$ to longer wavelength on passing through the sequence *trans-trans*, *trans-cis*, and *cis-trans* to *cis-cis*. This is now well established for conjugated dienes,[15] trienes,[15] and tetraenes [16] and contraverts Zechmeister's generalisation [17] based on compounds of the carotenoid type. The decline in $\varepsilon_{max.}$ is also in agreement with previous data. Although infrared curves were recorded for the 3-nitrophthalates of the hexadienols, Butenandt and his colleagues only report data for the 10 μ region for the alcohols themselves. We find that the bands in the C=C stretching

[9] Reichstein, Ammann, and Trivelli, *Helv. Chim. Acta*, 1932, **15**, 261 ; Nystrom and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 2548.
[10] Eisner, Elvidge, and Linstead, *J.*, 1953, 1372.
[11] Claisen, *Ber.*, 1911, **44**, 1161.
[12] Viguier, *Compt. rend.*, 1909, **149**, 403; *Ann. Chim.* (*France*), 1913, **28**, 433.
[13] Lunt and Sondheimer, *J.*, 1950, 3361.
[14] Crombie, Harper, and Newmann, *J.*, 1956, 3963.
[15] See Crombie and Jacklin, *J.*, 1957, 1632, for references.
[16] Holme, Jones, and Whiting, *Chem. and Ind.*, 1956, 928.
[17] Zechmeister, *Experientia*, 1954, **10**, 1.

region resemble those of the stereoisomeric deca-2 : 4-dienols [1] in that the doublet due to vibrational interaction moves progressively to lower frequencies and the frequency difference increases through the stereochemical sequence given above (Table 2). The *trans*-2 : *trans*-4-alcohol shows the expected strong band at 987 cm.$^{-1}$ but there is also weak absorption at 950 cm.$^{-1}$. As expected,[18] the *trans*-2 : *cis*-4-form has a pair of bands at 982 and 947 cm.$^{-1}$, and the *cis*-2 : *trans*-4-form has them at 986 and 952 cm.$^{-1}$. There is also a maximum or shoulder between 1003 and 999 cm.$^{-1}$ in all three of the above compounds and a somewhat similar situation is found in the decadienols. Beyond small inflexions on the skirt of the band with its maximum at 1015 cm.$^{-1}$, there are no maxima in the spectrum of the *cis*-*cis*-isomer in this region.

Experimental

Ultraviolet data were determined in EtOH with a Unicam S.P. 500 instrument.

Hex-cis-4-*en*-2-*yn*-1-*ol*.—A Grignard reagent was prepared from magnesium (28 g.) and ethyl bromide (128 g.) in anhydrous ether (250 ml.) and cooled to 0°, and *cis*-pent-3-enyne [5, 6] (76 g.) in anhydrous ether (100 ml.) was added with stirring during 2 hr. The mixture was heated under reflux for 90 min. with stirring, then cooled to 0°, and paraformaldehyde (45 g.; dried over P_2O_5) sublimed into the stirred solution in a current of dry nitrogen. The product was heated under reflux for 1 hr. and set aside for 12 hr. Iced sulphuric acid (700 ml.) was then added with cooling. The ethereal layer was separated and the aqueous layer extracted with ether. The united ethereal solutions were washed with sodium hydrogen carbonate solution, dried ($MgSO_4$), and evaporated to give *hex*-cis-4-*en*-2-*yn*-1-*ol* (40 g., 36%), b. p. 84—84·5°/18 mm., n_D^{20} 1·5016—1·5020. A second preparation (51% yield) had n_D^{20} 1·5006—1·5009 (Found: C, 74·6; H, 8·6. C_6H_8O requires C, 74·95; H, 8·4%). Light absorption: max. 225 mμ (ε 12,100). The α-*naphthylurethane* crystallised in needles [from light petroleum (b. p. 60—80°)], m. p. 110—111° (Found: C, 76·6; H, 5·7. $C_{17}H_{15}O_2N$ requires C, 76·95; H, 5·7%). On hydrogenation *cis*-hexenynol absorbed 3·0 H_2: the α-naphthylurethane of the product had m. p. 58° undepressed by an authentic sample of *n*-hexyl α-naphthylurethane.

Hex-trans-4-*en*-2-*yn*-1-*ol*.—In one run, use of the procedure described for the *cis*-isomer with *trans*-pent-3-enyne [5, 6] (20 g.), gave *hex*-trans-4-*en*-2-*yn*-1-*ol* (7·5 g., 27%), b. p. 87—89°/23 mm. In a second run on the same scale, the condenser became blocked with paraformaldehyde and the latter may have been added under slight pressure. This gave 48·0 g. of product (72%), b. p. 89—91°/25 mm. The final complex was orange whereas that from *cis*-pentenyne was colourless. The two products were united and redistilled, to give hex-*trans*-4-en-2-yn-1-ol (52 g.), b. p. 90·5—91·5°/22 mm., n_D^{20} 1·5037—1·5039 (Found: C, 74·9; H, 8·6%). Light absorption: max. 225 mμ (ε 12,500). The α-*naphthylurethane* formed clusters of needles, m. p. 114—115°, depressed to 73—76° when admixed with the derivative of the *cis*-isomer (Found: C, 77·4; H, 5·85%). On hydrogenation *trans*-hexenynol absorbed 3·0 H_2, to give *n*-hexanol which was characterised as *n*-hexyl α-naphthylurethane, m. p. and mixed m. p. 58°.

Hexa-trans-2 : trans-4-*dien*-1-*ol*.—Hex-*trans*-4-en-2-yn-1-ol (4·8 g.) in anhydrous ether (10 ml.) was added dropwise and with stirring to powdered lithium aluminium hydride (1·2 g.) suspended in ether (20 ml.). The mixture was stirred and heated under reflux for 3 hr., then cooled in ice and cautiously decomposed with water and then 2N-sulphuric acid (60 ml.). The ethereal layer was separated, washed with sodium hydrogen carbonate solution, dried ($MgSO_4$), and evaporated. Distillation gave hexa-*trans*-2 : *trans*-4-dien-1-ol (3·5 g., 73%), b. p. 82—83°/18 mm., m. p. 22° without recrystallisation (Found: C, 72·9; H, 10·25. Calc. for $C_6H_{10}O$: C, 73·4; H, 10·3%). Microhydrogenation: 2·0H_2. The α-naphthylurethane crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 98—99°, undepressed by an authentic specimen (below).

Hexa-trans-2 : cis-4-*dien*-1-*ol*.—Hex-*cis*-4-en-2-yn-1-ol (4·8 g.) was reduced with lithium aluminium hydride as described for the *trans*-compound to give hexa-*trans*-2 : *cis*-4-dien-1-ol (4·0 g., 83%), b. p. 83—84°/17 mm., n_D^{20} 1·5000—1·5003 (Found: C, 73·6; H, 10·5%). Microhydrogenation: 2·0 H_2. The α-naphthylurethane had m. p. 100—101° alone or mixed with the specimen described below.

Hexa-cis-2 : trans-4-*dien*-1-*ol*.—Hex-*trans*-4-en-2-yn-1-ol (4·9 g.) was shaken for 1 hr. with

[18] See refs. 1 and 2 for literature.

XUM

Raney nickel (*ca.* 1 g.) in methyl acetate. The nickel was filtered off and washed with methyl acetate, Lindlar's catalyst (1·5 g.) and quinoline (0·2 g.) were added to the filtrate, and the whole was shaken in hydrogen until hydrogen (1150 ml.) had been absorbed (calc. for 1 H_2, 1230 ml.). The catalyst was filtered off, the solvent removed *in vacuo*, and the residue distilled, to give hexa-*cis*-2 : *trans*-4-dien-1-ol (1·35 g., 27%), b. p. 79—80·5°/15 mm., n_D^{20} 1·4942—1·4951 (Found : C, 72·8; H, 10·15%). Microhydrogenation : 2·0 H_2. The α-naphthylurethane had m. p. and mixed m. p. 96·5—97·5°.

Hexa-cis-2 : cis-4-*dien*-1-*ol*.—Hex-*cis*-4-en-2-yn-1-ol (4·9 g.) was pre-treated with Raney nickel (1 g.) in ethyl acetate as above, then filtered, and the nickel washed. Lindlar catalyst (1·0 g.) and quinoline (0·2 g.) were added to the filtrate plus washings, and the mixture hydrogenated until 1130 ml. of gas had been absorbed (calc. for 1 H_2, 1210 ml.). Working up, and two distillations, gave hexa-*cis*-2 : *cis*-4-dien-1-ol (0·6 g., 12%), b. p. 79—81°, n_D^{20} 1·4840—1·4850 (Found : C, 73·7; H, 10·4%). Microhydrogenation : 2·0 H_2. The α-naphthylurethane had m. p. 88·5—89·5°.

Hexa-trans-2 : trans-4-*dien*-1-*ol*.—Reduction of ethyl sorbate (21·5 g.) in ether (50 ml.) by adding the solution to lithium aluminium hydride (3·0 g.) in ether (150 ml.) and working up in the usual way gave hexa-*trans*-2 : *trans*-4-dien-1-ol (12·8 g., 85%), b. p. 81·5—82·5°/14 mm., m. p. 28·5—29°. The α-naphthylurethane had m. p. 99·5—100° (lit.,[3,9] m. p. 30·5—31·5°; α-naphthylurethane, m. p. 100·5°).

Hexa-cis-2 : trans-4-*dien*-1-*ol*.—Hexa-cis-2 : *trans*-4-dienoic acid was prepared from δ-hexenolactone by the method of Eisner, Elvidge, and Linstead.[10] The lactone (22·4 g.), added to sodium (4·6 g.) in absolute methanol (700 ml.) at 15°, gave, on working up, methyl hexa-*cis*-2 : *trans*-4-dienoate (0·95 g., 5%), b. p. 64—65°/13 mm., n_D^{20} 1·4954—1·4956, and hexa-*cis*-2 : *trans*-4-dienoic acid (16 g., 71%). The latter (m. p. 28°) was not further purified, but added in dry ether (100 ml.) to lithium aluminium hydride (5·45 g.) in ether (200 ml.) at such a rate as to maintain gentle refluxing. After decomposition with water and 3N-sulphuric acid, the product was worked up in the usual way, to give hexa-*cis*-2 : *trans*-4-dienol (7·63 g., 54%), b. p. 70—72°/9 mm., n_D^{20} 1·4955—1·4964 (Found : C, 72·8; H, 10·2%). The 3 : 5-*dinitrobenzoate* crystallised from light petroleum (b. p. 60—80°) in yellow plates, m. p. 86—86·5° (Found : C, 53·2; H, 4·15. $C_{13}H_{12}O_6N_2$ requires C, 53·4; H, 4·15%). The *phenylurethane* crystallised in plates, m. p. 62·5—63·5° (Found : C, 71·8; H, 7·05. $C_{13}H_{15}O_2N$ requires C, 71·9; H, 6·95%). The α-naphthylurethane had m. p. 96—97°. On hydrogenation the diene alcohol absorbed 2·0 H_2, to give *n*-hexanol (α-naphthylurethane, m. p. and mixed m. p. 58°). Butenandt *et al.*[3] give b. p. 50—52°/3—5 mm., and α-naphthylurethane, m. p. 98—99·5°.

1 : 1-*Diethoxybut*-2-*yne*.—Redistilled crotonaldehyde (250 g.) was stirred and cooled in ice, and then bromine (185 ml.) was added during 90 min. Finally crotonaldehyde (3·6 g.) was added to decolorise the product. Anhydrous potassium acetate (425 g.) was added in portions with stirring, at <30°, and the product stirred for 1 hr. Water (100 ml.) was added and the mixture steam-distilled. The heavy layer which separated from the distillate was extracted with ether and the extract washed with portions of sodium carbonate solution. The extract was dried, washed, and distilled, to give α-bromocrotonaldehyde (323 g., 60%), b. p. 57—59°/10 mm. Dry ethanol (380 ml.), ethyl orthoformate (355 g.), and concentrated hydrochloric acid (4 ml.) were added to the aldehyde. Reaction began at once, the temperature rising to 55°. As soon as the temperature began to fall, the excess of ethyl orthoformate and the ethanol were distilled off through a short Vigreux column. Anhydrous sodium carbonate (6 g.) was added to the residue, which was filtered and distilled, to give α-bromocrotonaldehyde diethyl acetal (394 g., 82%), b. p. 82—84°/10 mm., n_D^{20} 1·4580 (Viguier [12] gives b. p. 86°/15 mm., n_D^{21} 1·4565).

The acetal (394 g.) was heated under reflux for 2½ hr. with potassium hydroxide (140 g.) in methanol (1·5 l.). The methanol was distilled off through a short column and water added to the residue. The organic layer was separated with the aid of ether, dried, evaporated, and distilled, to give 1 : 1-diethoxybut-2-yne (217 g.), b. p. 65—67°/12 mm., n_D^{20} 1·4296. A further 12 g. of this product were obtained by subjecting the distillation residue to further alkaline hydrolysis. The overall yield was 44% : runs on a 7-molar scale gave 40—42% yields. The method is well suited for large-scale work.

1 : 1-Diethoxybut-2-yne (48% yield in two experiments) was also prepared by Lunt and Sondheimer's method [13] and had b. p. 56—59°/9 mm., n_D^{20} 1·4285. The latter authors give b. p. 62—63·5°/14 mm., n_D^{20} 1·4290, and claim a yield of 80%.

XUM

But-2-yn-1-al.—1 : 1-Diethoxybut-2-yne (40 g.) was shaken for 12 hr. under nitrogen with saturated aqueous tartaric acid (40 ml.) and quinol (0·15 g.). Saturated calcium chloride solution (180 ml.) was added and after 3 minutes' shaking the product was extracted four times with ether. Drying, evaporation (short column), and distillation gave but-2-yn-1-al (4·9 g., 26%), b. p. 105—108°, n_D^{20} 1·4468. Acetal (15·0 g., 37·5%) was recovered. In our hands, yields of aldehyde have varied between 26 and 39%. Lunt and Sondheimer [13] give b. p. 105—110°, n_D^{20} 1·4456, average yield 35%.

*Ethyl 3-Hydroxyhex-*cis*-4-enoate.*—Zinc wool (5 g.) was activated by brief immersion in 2N-hydrochloric acid, washed with water, alcohol, acetone, and ether, and dried at 100°. The zinc was covered with dry benzene (10 ml.) and heated under reflux. A mixture of but-2-ynal (4·9 g.), ethyl bromoacetate (12·0 g.), and benzene (10 ml.) was added in portions (reaction began about 5 min. after the first addition). Then the mixture was stirred and heated under reflux for 1 hr., cooled in ice, and stirred for 1 hr. with 10% acetic acid (60 ml.). The benzene layer was separated, dried ($MgSO_4$), evaporated, and distilled, to give ethyl 3-hydroxyhex-4-ynoate (3·06 g., 27%), b. p. 70—71°/0·1 mm., n_D^{20} 1·4572.

The ester (2·34 g.) was hydrogenated at 5% palladium–barium sulphate (0·25 g.) in methyl acetate (5 ml.) until 1 mol. of hydrogen had been absorbed. Filtration, evaporation, and distillation gave *ethyl 3-hydroxyhex-*cis*-4-enoate*, (1·99 g., 84%), b. p. 59—59·5°/0·06 mm., n_D^{20} 1·4469 (Found : C, 60·5; H, 9·4. $C_8H_{14}O_3$ requires C, 60·7; H, 8·9%.)

*Dehydration of Ethyl 3-Hydroxyhex-*cis*-4-enoate.*—(i) The hydroxy-ester (0·9 g.) was heated to 170° for 1 hr. in nitrogen with powdered potassium hydrogen sulphate (0·76 g.). The product was cooled, water (5 ml.) added, and the organic layer removed by extraction with ether. The extract was dried, evaporated, and distilled (0·1 g.; b. p. 84—86°/12 mm., n_D^{20} 1·4950). Its infrared spectrum showed that it was mainly ethyl hexa-*trans*-2 : *trans*-4-dienoate.

(ii) The hydroxy-ester (0·4 g.) was heated under reflux for 1 hr. with benzene (1 ml.), pyridine (1 ml.), and phosphorus oxychloride (0·7 g.). The product was diluted with benzene (2 ml.) and washed successively with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water, then dried ($MgSO_4$), and the benzene evaporated. Distillation gave an ester (0·12 g.), b. p. 83—84°/14 mm., n_D^{20} 1·4926. Light absorption : max. 258 mμ (ε 29,200). The infrared spectrum showed it to be almost pure ethyl hexa-*trans*-2 : *trans*-4-dienoate.

(iii) The hydroxy-ester (4·2 g.) was mixed with phosphoric oxide (4·5 g.); reaction set in and the mixture became brown. Removal of the product *in vacuo* and redistillation gave an ester, b. p. 77—78°/9 mm., n_D^{20} 1·4870—1·4900. Light absorption : max. 258 mμ (ε 23,700). The infrared absorption showed it to contain large amounts of ethyl hexa-*trans*-2 : *trans*-4-dienoate.

*Ethyl Hex-*trans*-2-en-4-ynoate.*—Ethyl 3-hydroxyhex-4-ynoate (6·7 g.) was mixed with phosphoric oxide (5 g.); heat was produced and the mixture became brown. Distillation gave a product, b. p. 78—82°/9 mm., n_D^{20} 1·4940, which when redistilled gave ethyl *hex-*trans*-2-en-4-ynoate* (2·34 g., 39%), b. p. 79·5—81°/9 mm., n_D^{20} 1·4958—1·4962 (Found : C, 68·7; H, 7·0. $C_8H_{10}O_2$ requires C, 69·5; H, 7·3%). Microhydrogenation : 3·0 H_2. Light absorption : max. 257 mμ (ε 19,000). For preparative work, phosphoric oxide was heated to 130° *in vacuo* and an equal weight of ethyl 3-hydroxyhex-4-ynoate added dropwise; the enyne ester distilled continuously. Redistillation of the crude product gave enyne ester (30—48%), b. p. 90—92°/12 mm., n_D^{20} 1·4963.

*Hexa-*trans*-2 :* cis*-4-dien-1-ol.*—Ethyl hex-*trans*-2-en-4-ynoate (23·4 g.) was hydrogenated in ethyl acetate (75 ml.) over Lindlar catalyst (7·0 g.) in the presence of quinoline (1·2 g.). Reduction was interrupted when hydrogen (3·72 l. at 17°/750 mm.) had been absorbed (calc. for absorption of 1 mol., 3·9 l.). Two careful fractionations gave ethyl hexa-*trans*-2 : *cis*-4-dienoate (13·4 g., 54%), b. p. 85·5—86·5°/18 mm., n_D^{20} 1·4858—1·4872. Light absorption : max. 261 mμ (ε 21,000). Microhydrogenation : 2·0 H_2. Allan *et al.*[2] give max. 262 mμ (ε 23,500) for the methyl ester.

The ethyl ester (13·2 g.) in anhydrous ether (50 ml.) was added during 90 min. to lithium aluminium hydride (3·35 g.) in ether (70 ml.) under nitrogen. After stirring (15 min.), ice-water was added cautiously and then 2N-sulphuric acid. Isolation in the usual way gave hexa-*trans*-2 : *cis*-4-dien-1-ol (7·32 g., 78%), b. p. 79—81°/15 mm., n_D^{20} 1·4982 (there was considerable frothing during the distillation) (Found : C, 73·0; H, 10·5%). Light absorption : max. 229 mμ (ε 18,400). The 3 : 5-*dinitrobenzoate* formed pale yellow leaflets, m. p. 73° (Found : C, 53·2; H, 4·3. $C_{13}H_{12}O_6N_2$ requires C, 53·4; H, 4·15%). The α-naphthylurethane had m. p. 99—100° (Found : C, 76·1; H, 6·7. Calc. for $C_{17}H_{17}O_2N$: C, 76·4; H, 6·4%). On microhydrogenation

2·0 H_2 were absorbed and the product was identified as *n*-hexanol (α-naphthylurethane, m. p. and mixed m. p. 59°).

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533. *Amides of Vegetable Origin. Part VIII.* The Constitution and Configuration of the Sanshoöls.*

By L. Crombie and J. L. Tayler.

The insecticidal extract of *Zanthoxylum piperitum* DC. bark contains an unstable lipid *iso*butylamide (m. p. 69°) possessing a conjugated triene system. As Aihara's sanshoöl I is probably an impure form of it, the substance is referred to as α-sanshoöl. On hydrogenation the amide absorbs 4 mols. of hydrogen and gives *N-iso*butyldodecanamide. Oxidative degradation yields *N-iso*butyloxamic acid, succinic acid, and acetaldehyde, and this, with supporting spectroscopic evidence, shows it to be *N-iso*butyldodeca-2 : 6 : 8 : 10-tetraenamide : it appears to be identical with *neo*herculin.

Iodine-catalysed stereomutation of α-sanshoöl gives a higher-melting β-form. Both α- and β-sanshoöl form adducts with maleic anhydride and the spectra of these, and the parent compounds, show that α-sanshoöl has a 2-*trans*-linkage and a *cis-trans-trans*-triene system, whilst the β-form is all-*trans*. The orientation of the triene unit is demonstrated by oxidising the maleic anhydride adduct of α-sanshoöl to succinic acid. α-Sanshoöl is thus *N-iso*butyldodeca-*trans*-2 : *cis*-6 : *trans*-8 : *trans*-10-tetraenamide. Sanshoöl II may be the β-form of this structure.

The lignan (−)-sesamin has been isolated from *Z. piperitum* bark.

Recent synthetical investigation [1] has shown that either sanshoöl I has not the gross structure (I) assigned to it by Aihara,[2] or else it is a very impure substance. Two stereoisomers of (I), *trans*-2 : *trans*-4 : *trans*-8 and *trans*-2 : *trans*-4 : *cis*-8, were synthesised and

$$Me\cdot[CH_2]_3\cdot CH{=}CH\cdot[CH_2]_3\cdot CH{=}CH\cdot CH{=}CH\cdot CO\cdot NHBu^i \quad (I)$$

it became apparent that further work in this direction would be unrewarding until the natural insecticidal amides of *Zanthoxylum piperitum* DC. had been re-investigated. Through the efforts of Mr. T. Akiyama of the Japanese Embassy in London, a supply of the bark of this tree has become available to us and we now report our findings.

Aihara isolated sanshoöl I by methanol extraction followed by a series of purifications involving three vacuum-distillations.[2] We have used extraction with light petroleum (b. p. 40—60°) followed by partition of the extract with nitromethane. The nitromethane solution was purified, then evaporated *in vacuo*, and the residue chromatographed on neutral alumina from light petroleum and ether. This procedure gave a rapidly eluted fraction containing insecticidal and sialogogue *iso*butylamides and later fractions containing a non-sialogogue crystalline substance, m. p. 121—123°. Aihara [2] reports that he encountered a similar substance but threw no light on its constitution.

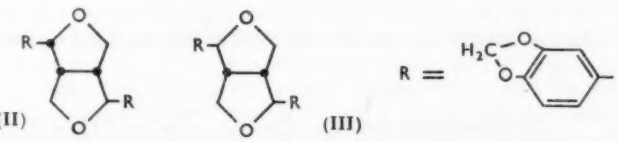
The substance of m. p. 121—123° gave analyses correct for $C_{20}H_{18}O_6$ and had ultraviolet maxima at 237 (ε 9100) and 286 mμ (ε 8200). These results suggested that it might

* Part VII, *J.*, 1955, 4244.

[1] Crombie and Shah, *J.*, 1955, 4244.

[2] Aihara, *J. Pharm. Soc. Japan*, 1950, **70**, 405 [No. 7—8, p. 43]. This paper gives references to the earlier literature; cf. also *idem, ibid.*, 1951, **71**, 1112.

be the lignan (−)-asarinin (II),* which has m. p. 121—122° and ultraviolet maxima at 237 (ε 9300) and 287 mμ (ε 8700),[3] for (−)-asarinin has been isolated from the bark of the related tree *Z. clava-herculis* L.[4, 5] On admixture, however, the m. p. was heavily depressed, and the infrared spectra of the two compounds were very different though no differences in functional groupings could be deduced. The rotation was $[\alpha]_D^{24}$ −65° [(−)-asarinin has $[\alpha]_D^{18}$ −125°], and this led us to suspect that it might be (−)-sesamin (III),† a stereoisomer of (−)-asarinin with m. p. 121—122°, $[\alpha]_D^{18}$ −69°.[6] A specimen of (−)-sesamin was prepared by stereoequilibrating natural (−)-asarinin with alcoholic hydrogen chloride and fractionally crystallising the product.[6] It was identical with the lignan from *Z. piperitum* (mixed m. p. and infrared spectrum). (−)-Sesamin is reported [7] to occur in another natural source, *Asarum sieboldii* Miquel.



The amide fraction obtained by chromatography was purified by repeated crystallisation and eventually gave a very unstable lipid amide, $C_{16}H_{25}ON$, m. p. 69°, subsequently referred to as α-sanshoöl. When it was hydrogenated over Adams catalyst an octahydro-derivative was produced identical with *N-iso*butyldodecanamide. The infrared

TABLE 1.

	$\lambda_{max.}$ (mμ)	ε
α-Sanshoöl [*cis*-6 : *trans*-8 : *trans*-10]	260	36,000
	269	47,000
	278·5	37,500
α-Elæostearic acid [*cis*-9 : *trans*-11 : *trans*-13] [a]	261	36,000
	271	47,000
	281	38,000
β-Elæostearic acid [*trans*-9 : *trans*-11 : *trans*-13] [a,c]	259	47,000
	268	61,000
	279	49,000
Punicic acid [*cis*-9 : *trans*-11 : *cis*-13] [b]	264	35,000
	274	46,000
	285	34,500

[a] Crombie and Tayler, *J.*, 1954, 2816. [b] Crombie and Jacklin, *J.*, 1957, 1632. [c] The *N-iso*butylamide has maxima at 258, 268, and 278 mμ (ε 42,000, 58,500, and 43,500): see Part IX.

spectrum of α-sanshoöl indicated that an α-unsaturated amide function was present and the ultraviolet light absorption (Table 1) gave strong evidence for a conjugated triene system. The ultraviolet data also support the presence of an α-unsaturated amide group as ε at 230 mμ (not a max.) is 12,500 whereas at this wavelength the normal residual absorption of a triene (represented by α-elæostearic acid) is ~4000. *N-iso*Butyldeca-*trans*-2 : *trans*-6-dienamide has ε 10,000 at 230 mμ. A similar conclusion can be drawn from the maleic anhydride adduct of α-sanshoöl in which the triene absorption is destroyed: it has ε 8000 at 230 mμ.

On oxidation with permanganate, *N-iso*butyloxamic acid was isolated, and ozonolysis

* The geometrical configurations are those assigned by Erdtmann and Pelchowicz (*Chem. and Ind.*, 1955, 567) and Beroza (*J. Amer. Chem. Soc.*, 1956, **78**, 5082); absolute configurations, which are not known, are not to be implied from formulæ (II) and (III).

[3] Aulin-Erdtmann and Erdtmann, *Svensk Papperstidn.*, 1944, **47**, 22.

[4] *Inter alia*, Colton, *Amer. J. Pharm.*, 1890, 191; Gordin, *J. Amer. Chem. Soc.*, 1906, **28**, 1648; Dieterle and Schwengler, *Arch. Pharm.*, 1939, **277**, 33.

[5] Crombie, *J.*, 1952, 2997.

[6] Huang-Minlon, *Ber.*, 1937, **70**, 951.

[7] Kaku and Ri, *Keijo J. Med.*, 1938, **9**, 1—4 (*Chem. Abs.*, 1938, **32**, 9089).

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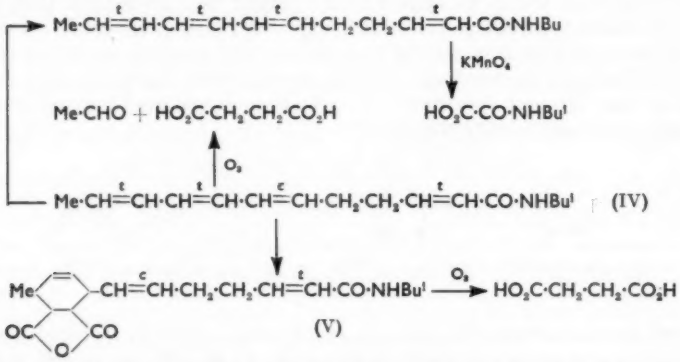
gave acetaldehyde (2 : 4-dinitrophenylhydrazone) and succinic acid : the last two fragments were identified by paper chromatographic techniques. Because material was scarce, the permanganate oxidation was actually carried out on the stereoisomeric β-form (see below). It follows that α-sanshoöl is (IV) and its gross structure is the same as that of *neo*herculin.[8] Although direct comparison cannot be made until fresh *neo*herculin has been



isolated it is almost certain from m. p.'s and ultraviolet and infrared data, coupled with the similar general behaviour, that the two substances are identical. There also seems a possibility that the lipid *iso*butylamide, echinacein (m. p. 63—64°), recently isolated from *Echinacea angustifolia* DC.,[9] may be the same as α-sanshoöl, for, unless rigorously purified, specimens of the latter (and of *neo*herculin) tend to melt about 5° low. Echinacein gives *N-iso*butyldodecanamide on hydrogenation though other degradative evidence is not available beyond the report of a maximum at 259 mμ which is said [9] to be due to a triene system (the other members of the triplet are not mentioned). It is a sialogogue and an insecticide.

Aihara's sanshoöl I,[2] melting near room temperature, seems to have been a very impure specimen of α-sanshoöl. The ultraviolet maximum at 267·5 mμ (ε 33,000), which cannot be due to a 5-monosubstituted *N-iso*butylpenta-2 : 4-dienamide type of chromophore as he thought,[1] corresponds to that of an impure triene, and the absence of the bands at 260 and 278·5 mμ, together with the presence of a considerable long-wavelength inflexion, can be accounted for if much impurity were present. Aihara's sample absorbed 3·24 mols. of hydrogen to give *N-iso*butyldodecanamide and on oxidative degradation produced *N-iso*-butyloxamic acid and succinic acid, though the reported *n*-butyric acid is not accounted for.

The configuration of *neo*herculin has been discussed in a previous paper,[8] but, on the data then available, could only be partly defined. The matter has been further examined by using α-sanshoöl. As before, the position of the CH=CH stretching vibration (1668 cm.$^{-1}$, intense because of conjugation with a carboxyamide grouping) suggests that it is a *trans*-structure and further evidence is forthcoming below. Ultraviolet data for the triene linkage (Table 1) indicate that it has probably *cis-trans-trans*-configuration; on addition of iodine there is a slight shift of the main maximum to 268 mμ and ε increases to 55,000. This parallels the behaviour of α-elæostearic (octadeca-*cis*-9 : *trans*-11 : *trans*-13-trienoic) acid which is similarly isomerised to the β(all-*trans*)-form. Support for validity of this analogy is given by the isolation of a maleic anhydride adduct (V) from α-sanshoöl by reaction in benzene at 100° : this is evidence for two contiguous *trans*-linkages in the triene. An earlier attempt to obtain an adduct from *neo*herculin failed, and on these grounds it had been tentatively proposed that such an arrangement was absent.[8] * β-Sanshoöl also

* *Added, April 29th*, 1957.—We have since obtained this adduct from *neo*herculin.

[8] Crombie, *J.*, 1955, 995; *Nature*, 1954, **174**, 833.
[9] Jacobson, *Science*, 1954, **120**, 1028.

gives a maleic adduct which, by analogy with β-elæostearic acid, may be a mixture involving addition across both the 6 : 9- and the 8 : 11-positions.[10] The two sanshoöl adducts differ in that the β-form has a band at 967 cm.$^{-1}$ (also present in the maleic adduct of *N-iso*butyl-β-elæostearamide at 967 cm.$^{-1}$) which is not found in the α-isomer; this is in the correct position for an unconjugated *trans*-double bond (out-of-plane deformation vibration) and is convincingly ascribed to the double bond of the all-*trans*-triene not involved in adduct formation.[11] In the α-form, this double bond must be *cis*.

Further stereochemical evidence comes from infrared spectra paraffin mull of α- and β-sanshoöl in the 1000—950 cm.$^{-1}$ region. α-Elæostearic acid has bands at 991 and 698 cm.$^{-1}$ characteristic of the *cis-trans-trans*-triene; on stereomutation these are replaced by a strong band at 987 cm.$^{-1}$. α-Sanshoöl has bands at 994 and 972 cm.$^{-1}$ agreeing with the *cis-trans-trans*-configuration, but, if our deduction that the 2-unsaturation is *trans* is correct, there ought in any case to be a band at 977 cm.$^{-1}$.[5,12] Consequently the band at 972 cm.$^{-1}$ should be composite. Evidence that this is so is forthcoming from semiquantitative extinction measurements (carbon tetrachloride solution) as the band is about three times stronger than that of the corresponding band in elæostearic acid. β-Sanshoöl shows the expected all-*trans*-triene band at 996 cm.$^{-1}$ with a strong inflexion at 978 cm.$^{-1}$ which is in the correct position for the *trans*-2-double bond. (This vibration occurs at 977 cm.$^{-1}$ in *N-iso*butyldec-*trans*-2-enamide.[5]) It is also significant that the maleic anhydride adducts of α- and β-sanshoöl have bands at 978 (α) and 980 (β) cm.$^{-1}$ which are absent in the adduct from *N-iso*butyloctadeca-*trans*-9 : *trans*-11 : *trans*-13-trienamide (no 2-unsaturation) : these can be assigned to the above structural feature.

The evidence above determines the position of the olefinic linkages and the configuration of the 2-double bond and the 6 : 8 : 10-triene system in α-sanshoöl. It does not establish the orientation of the *cis-trans-trans*-system. This was determined by oxidising the maleic anhydride adduct of α-sanshoöl with ozone and hydrogen peroxide. Succinic acid, which could come only from (V), and not from a product of addition to the 6 : 8-linkages, was obtained in 55% yield and detected and estimated by a paper-chromatographic method. The structure (IV), *N-iso*butyldodeca-*trans*-2 : *cis*-6 : *trans*-8 : *trans*-10-tetraenamide, agrees with all the known facts about α-sanshoöl.

During the isolation of lipid amides from *Z. piperitum* bark, sanshoöl II, described by Aihara [13] as a very unstable substance softening at 114° and finally melting at 125—126°, was never found. The substance, according to the Japanese author, analyses as $C_{16}H_{25}ON$, absorbs four mols. of hydrogen to give *N-iso*butyldodecanamide, and on oxidation yields acetic, succinic, and *N-iso*butyloxamic acid. Aihara [13] gave sanshoöl II the structure (VI) but again the light absorption data (max. 267·5 mμ, ε 33,000) are more consistent with

$$Me{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CH{=}CH{\cdot}CH{=}CH{\cdot}CO{\cdot}NHBu^i \quad \text{(VI)}$$

an impure conjugated triene than with a 5-monosubstituted *N-iso*butylpenta-2 : 4-dienamide (max. 258—259 mμ). Our gross structure (IV) is fully consistent with Aihara's data and we suggest that sanshoöl II may be the β(all-*trans*)-form, obtained by thermal stereomutation of the α-form during the distillation processes. Although we have not been able to spare our best specimens of α-sanshoöl for isomerisation, material of m. p. 63—66° has given β-form of m. p. 110—115° on irradiation in the presence of a trace of iodine. The substance, although crystallising in rosettes of excellent needles, is unstable and very difficult to purify. We have never handled a pure sample, and spectroscopic data obtained on the β-form were obtained with the above material. When the crude crystallisation residues from α-sanshoöl preparations were treated with iodine, considerable amounts of still less pure β-form could be isolated. The *N-iso*butyldodecanamide formed

[10] Bickford, Dupré, Mack, and O'Connor, *J. Amer. Oil Chemists' Soc.*, 1953, **30**, 376.
[11] Cf. Paschke, Tolberg, and Wheeler, *ibid.*, 1953, **30**, 97.
[12] Crombie, *J.*, 1952, 4338.
[13] Aihara, *J. Pharm. Soc. Japan*, 1950, **70**, 409 [No. 7—8, p. 47].

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from the latter by hydrogenation is not completely pure, and contamination by amides of different chain length seems to be involved. On ozonolysis the crude β-material gave mainly acetaldehyde together with smaller amounts of longer-chain aldehydes.

Experimental

Analyses were carried out in the Microanalytical (Miss J. Cuckney) and infrared measurements in the Spectroscopic Laboratories (Mr. R. L. Erskine) of this Department. A Grubb-Parsons double-beam instrument with rock-salt optics was used. Unless otherwise stated, solid substances were examined as paraffin mulls. Ultraviolet absorption data were obtained with pure ethanol as solvent.

Isolation of α-Sanshoöl and (−)-Sesamin.—Ground bark of *Z. piperitum* (2·7 kg.) was extracted with light petroleum (b. p. 40—60°) in a semicontinuous process in which, after soaking (24 hr.) the extract was drawn off into a pot and two-thirds of the petroleum redistilled into the extractor. Eight such soakings were given and heating of the extracts kept to a minimum. The greenish-yellow total extract remaining in the pot was concentrated to 1 l. and partitioned with portions of nitromethane (1 × 300, 1 × 200, and 5 × 100 ml.). Evaporation of the greenish-yellow nitromethane extract under reduced pressure gave a dark green oil which was dissolved in ether (300 ml.) and washed with 2N-sodium hydroxide, 2N-sulphuric acid, and then water. The ethereal solution was dried (Na_2SO_4) at 3°, and evaporated to a greenish oil (33 g., 1·2%) (Aihara [3] found 1·1% of methanol extractive).

The oil was dissolved in 1 : 1 light petroleum (b. p. 40—60°)–ether and chromatographed on neutral alumina. The fractions which were rapidly eluted contained lipid *iso*butylamides and their progress could be followed from the sialogogue effect of material leaving the column. After evaporation, this group of fractions was crystallised four times, with cooling, where necessary, to sub-zero temperatures, to give impure α-sanshoöl (717 mg., 0·03%), m. p. 63—66°. The next group of fractions was set aside at 0° for several days and deposited crude (−)-sesamin (1 g., 0·04%) which had m. p. 120° (sintering from 84°), raised by repeated crystallisation from ethanol to m. p. 121—123°. The substance was not a sialogogue. Later fractions from the chromatogram (eluted with pure ether) yielded a yellow oil (1 g.) which was not a sialogogue and was not examined further.

When the residues from the crystallisation of α-sanshoöl were treated under light petroleum with iodine, crude β-sanshoöl (3 g.), m. p. 98° (unsharp), crystallised. The β-form was not encountered at any other stage of the working-up procedure. The crystallisation residues, before isomerisation, gave a 56% kill when tested against *Tenebrio molitor* as a 3% w/v solution according to a standard measured-drop technique.

α-Sanshoöl.—Repeated crystallisation of the crude product (above) from light petroleum (b. p. 40—60°) gave α-sanshoöl of m. p. 69°, separating from solution in a characteristic bulky form. *neo*Herculin has m. p. 69—70° and crystallises similarly [4] (Found: C, 77·85; H, 10·25; N, 5·65. Calc. for $C_{16}H_{25}ON$: C, 77·7; H, 10·2; N, 5·65%). Microhydrogenation 3·85 H_2. Light absorption see Table 1. Infrared bands were present at 3200m and 3060w (NH), 1668m (α-C=C), 1626s (amide carbonyl), 1560 (amide B), 994, and 972 cm.$^{-1}$ (*trans-trans-cis*-triene and *trans*-α-CH=CH). In carbon tetrachloride solution the apparent extinction coefficients at 992 and 964 cm.$^{-1}$ were 275 and 110 respectively. See Crombie and Jacklin [14] for comparative data. The m. p. of 69° above refers to the best sample obtained: others had m. p. 65—67° even after a considerable number of crystallisations. α-Sanshoöl must be kept sealed *in vacuo* at 0°. A 3% w/v solution, when tested against *T. molitor* by the above technique, gave a 77% kill.

β-Sanshoöl.—α-Sanshoöl (217 mg.; m. p. 63—66°) was dissolved in light petroleum (b. p. 40—60°; 20 ml.), a trace of iodine added, and the solution illuminated with a tungsten lamp. The crude β-form (200 mg.) crystallised in small needles of excellent form and after two crystallisations had m. p. 112°. Other samples of α-sanshoöl of similar quality gave products of m. p. 110—115°: the m. p. was not readily improved by crystallisation and in some cases deteriorated (Found: C, 77·15; H, 10·0; N, 5·6%). Light absorption max. 259, 267·5, and 278 mμ (ε 38,500,

[14] Crombie and Jacklin, *J.*, 1957, 1632.

48,500, and 39,000). Infrared bands: 3250m and 3060w (NH), 1667m (α-C=C), 1623s (amide carbonyl), 1549ms (amide B), 996s (all-*trans*-triene), and 978 cm.$^{-1}$ strong inflexion (*trans*-α-CH=CH). The β-form is a weaker sialogogue than the α-form: a 3% w/v solution in acetone, when tested against *T. molitor* as above, gave a 21% kill.

Hydrogenation of α-Sanshoöl.—The amide (209 mg.) was hydrogenated in ethyl acetate with 5% palladised carbon as catalyst: almost exactly 4 mols. of hydrogen were absorbed. The catalyst was filtered off and the solution evaporated, to give a solid, m. p. 48—49°, which when recrystallised from light petroleum (b. p. 60—80°) gave *N-iso*butyldodecanamide, m. p. 51—52·5°, undepressed by an authentic specimen of m. p. 51·5—53°.

Under similar conditions, crude β-sanshoöl (m. p. 103—112°; obtained by recrystallising β-material obtained from the crystallisation residues from the α-form) absorbed almost exactly 4 mol. of hydrogen. The product had m. p. 45—47° but the m. p. was not improved by five crystallisations. On admixture with *N-iso*butyldodecanamide, the m. p. was raised to 47—50°.

Oxidation Products of Sanshoöl.—(a) *Succinic acid.* α-Sanshoöl (49 mg.) was ozonised in glacial acetic acid (90 min.), 30% hydrogen peroxide (1·5 ml.) added, and the mixture set aside at 35° (2 days).[15] Water (20 ml.) was added and the solution extracted with light petroleum and then chloroform. The aqueous phase was carefully evaporated to dryness, the residue (oily solid) dissolved in ethanol, and a portion chromatographed on paper sheet according to the method of Cheftel and his co-workers [16] (development, ammoniacal ethanol: spraying reagents, bromocresol-green–lead acetate). A mixture of oxalic, malonic, and succinic acid was run on the same sheet for reference. Only one prominent spot, corresponding in R_F value to the succinic acid standard, was observed.

(b) *Acetaldehyde.* α-Sanshoöl (183 mg.) was ozonised in "AnalaR" glacial acetic acid (5 ml.) for 80 min. Zinc dust (2 g.) and water (30 ml.) were added, the mixture was heated to the b. p., and volatile aldehydes were steam-distilled into Brady's reagent. The precipitated 2 : 4-dinitrophenylhydrazone was filtered off, dissolved in benzene, and chromatographed on alumina (Brockmann grade III). The weakly absorbed zone was eluted; the 2 : 4-dinitrophenylhydrazone (30 mg.) recovered had m. p. 151°, raised by crystallisations to 158—160°. For identification, the derivative was chromatographed on paper sheet impregnated with olive oil, with *iso*propanol–water as the eluting solvent, according to Seligman and Edmonds's method.[17] The 2 : 4-dinitrophenylhydrazones of formaldehyde, acetaldehyde, and propionaldehyde were chromatographed as reference substances. Only one prominent spot, corresponding to acetaldehyde 2 : 4-dinitrophenylhydrazone, was obtained though traces of two other 2 : 4-dinitrophenylhydrazones were noted. When ozonised by the same technique, crude β-sanshoöl (above) gave mainly acetaldehyde together with small amounts of higher aldehydes.

(c) N-iso*Butyloxamic acid.* Crude β-sanshoöl (445 mg.) was dissolved in aqueous acetone, and potassium permanganate (3 g.) added with shaking, at 50°. The product was filtered, concentrated, acidified, and steam-distilled to remove volatile acids. After neutralisation, the residue from the steam-distillation was concentrated to 50 ml. and then acidified and continuously extracted with ether. The extract was evaporated to a gummy solid from which *N-iso*butyloxamic acid was isolated by treatment with portions of hot light petroleum (b. p. 40—60°). The *N-iso*butyloxamic acid crystallised in white feathery needles, m. p. 104—106°, undepressed when admixed with an authentic specimen of m. p. 105—107°.

Maleic Anhydride Adduct of α-Sanshoöl.—α-Sanshoöl (326 mg.), maleic anhydride (130 mg.), and benzene (4 ml.) were mixed (a yellow colour developed at once) and heated in a sealed tube at 100° for 24 hr. On cooling, no crystals were deposited, so the benzene was evaporated leaving a yellow oil which solidified when triturated with ether and light petroleum (b. p. 60—80°). The white solid (273 mg.; m. p. 90—92°) was crystallised from ether–light petroleum to m. p. 99—100·5°: the *adduct* had a powdery appearance (Found: N, 3·95. $C_{20}H_{27}O_4N$ requires N, 4·05%). No high-intensity maximum was observed in the ultraviolet region above 210 mμ (ε values at 210 and 230 mμ were 16,000 and 8000). *N-iso*Butyldeca-*trans*-2 : *trans*-6-dienamide also showed no maximum in this range when examined with a photoelectric instrument (ε values at 210 and 230 mμ were 20,500 and 10,000). Previously, when the photographic method (Hilger medium quartz instrument) was used, a subsidiary maximum at 226 mμ on a rising curve was reported [5] for this and related α-unsaturated *iso*butylamides. For

[15] Cf. Klenk and Bongard, *Z. physiol. Chem.*, 1952, **290**, 181.
[16] Cheftel, Munier, and Macheboeuf, *Bull. Soc. Chim. biol.*, 1952, **34**, 380.
[17] Seligman and Edmonds, *Chem. and Ind.*, 1955, 1406.

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comments on similar discrepancies see Allan *et al.*[18] The infrared spectrum of α-sanshoöl–maleic anhydride adduct showed bands at 3295m and 3125w (NH), 1838mw and 1765s (anhydride), 1669m (α-C=C), 1618s (amide-carbonyl), 1543m (amide B) and 978m cm.$^{-1}$ (*trans*-α-CH=CH).

Under similar conditions β-sanshoöl gave an adduct which, after three crystallisations from ethyl acetate–light petroleum (b. p. 40—60°) or benzene–light petroleum, had m. p. 148—151° (Found: N, 3·9%). Infrared bands were present at 3280m and 3040w (NH), 1842m and 1768s (acid anhydride), 1664m (α-C=C), 1618s (α-unsaturated amide carbonyl), 1547m (amide B), 980m (*trans*-α-CH=CH), and 967m cm.$^{-1}$ (unconjugated *trans*-CH=CH). Compare the maleic adduct of *N-iso*butyloctadeca-*trans*-9 : *trans*-11-*trans*-13-trienamide which has bands at 1843m and 1770s (acid anhydride), 1645s (α-saturated amide carbonyl), 1547s (amide B), and 967m cm.$^{-1}$ (unconjugated *trans*-CH=CH).

Oxidation of α-Sanshoöl–Maleic Anhydride Adduct.—The maleic adduct (80 mg.) was ozonised for 1 hr. in glacial acetic acid, and the product treated with 30% hydrogen peroxide at 35° (48 hr.). The solution was concentrated, diluted and extracted with light petroleum (b. p. 40—60°) and then chloroform. The aqueous phase was evaporated under a vacuum, the residue dissolved in a known volume of ethanol, and an aliquot part chromatographed by the method of Cheftel *et al.*[16] Succinic acid was identified (~55% yield as determined by a spot-area technique [19]). A second large spot of R_F near to that of malonic acid was identified: since no malonic acid was obtained from α-sanshoöl itself, the spot is probably due to an acid formed by degradation of the *cyclo*hexane ring. It was not *N-iso*butyloxamic acid as the latter has an R_F value greater than that of succinic acid.

Identification of (−)-Sesamin.—(−)-Sesamin obtained from *Z. piperitum* bark had m. p. 121—123°, $[\alpha]_D^{24}$ −65° (*c*, 2·67% in $CHCl_3$) [Found: C, 67·55; H, 5·4; O (direct) 27·3%; *M* (Rast), 335. Calc. for $C_{20}H_{18}O_6$: C, 67·75; H, 5·1; O, 27·1%; *M*, 354·3]. See text for ultraviolet data. On admixture with (−)-asarinin the m. p. was depressed to 98—103°.

(−)-Asarinin, isolated from *Z. clava-herculis* bark,[5] had m. p. 121°, $[\alpha]_D^{21}$ −125° (*c* 2·90% in $CHCl_3$). The substance (5 g.) was stereoequilibrated according to Huang-Minlon's directions [6] under reflux (12 hr.) with 10% alcoholic hydrogen chloride. By fractional crystallisation of the product, (−)-sesamin, m. p. 120°, was isolated: it did not depress the m. p. of the above specimen and had an identical infrared spectrum. Recorded data [6] are m. p. 121—122°, $[\alpha]_D^{18}$ −68·9° (*c* 1·14% in $CHCl_3$).

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[*Received, December 19th*, 1956.]

[18] Allan, Jones, and Whiting, *J.*, 1955, 1862.
[19] Ackman, Linstead, and Weedon, unpublished work.

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534. *Amides of Vegetable Origin. Part IX.* Total Synthesis of Anacyclin and Related Trienediynamides.*

By L. Crombie and M. Manzoor-i-Khuda.

The structure proposed in Part IV for the natural amide anacyclin, *N-iso*butyltetradeca-*trans*-2 : *trans*-4-diene-8 : 10-diynamide, is confirmed by total synthesis. *N-iso*Butylnona-*trans*-2 : *trans*-4-dien-8-ynamide is first synthesised and then oxidatively cross-coupled with pent-1-yne. By partially hydrogenating synthetic anacyclin, *N-iso*butyltetradeca-*trans*-2 : *trans*-4 : *cis*-8 : *cis*-10-tetraenamide is isolated crystalline, with insecticidal activity. When *N-iso*butylnona-*trans*-2 : *trans*-4-dien-8-ynamide is cross-coupled with *cis*- and with *trans*-pent-2-en-4-yne, *N-iso*butyltetradeca-*trans*-2 : *trans*-4 : *cis*-12- and -*trans*-2 : *trans*-4 : *trans*-12-triene-8 : 10-diynamide are formed. These may be related to the contaminant of natural anacyclin which shows enediyne absorption in the ultraviolet region.

Infrared data reveal that maleic anhydride adducts of the above *N-iso*butyl-*trans*-2 : *trans*-4-dienamides are not anhydrides having a carboxyamide grouping but *N-iso*butylimides having a carboxylic acid group. This is established chemically by preparing the dihydro-adduct of *N-iso*butylsorbamide and maleic anhydride, identical with the dihydro-*N-iso*butylmaleimide adduct of 3-methylpenta-2 : 4-dienoic acid.

Anacyclin was recently isolated from the roots of *Anacyclus pyrethrum* DC. (pellitory) where it occurs with other insecticidal, unsaturated, lipid-*iso*butylamides.[1] The amide itself had little toxicity towards the grain insect *Tenebrio molitor*, but became potent after catalytic semihydrogenation of its two acetylenic linkages. Earlier work [1] indicated that it had structure (IX). This is now confirmed by a synthesis which has been summarised elsewhere.[2]

A necessary intermediate, hept-*trans*-2-en-6-yn-1-al (VI), has been described by Shaw and Whiting,[3] but we improved the reported yield (18%) of its precursor, hepta-2 : 6-diynoic acid, by employing " reversed addition "; the Grignard reagent from hexa-1 : 5-diyne, prepared by adding 1 mol. of ethylmagnesium bromide to the hydrocarbon, gave, after carboxylation, 34% of hepta-2 : 6-diynoic acid (on a small scale yields of up to 53% were obtained). When the diyne hydrocarbon was added to the Grignard reagent as described by Shaw and Whiting, and the product carboxylated, the yield of unwanted octa-2 : 6-diyndioic acid (II) increased considerably at the expense of hepta-2 : 6-diynoic acid (III). The latter could be converted satisfactorily into its methyl ester by diazomethane, though if the mixture was set aside with an excess of the reagent a crystalline pyrazole, arising from attack at the α-acetylenic linkage, could be isolated. Methyl or ethyl hepta-2 : 6-diynoate was reduced by lithium aluminium hydride to hept-*trans*-2-en-6-yn-1-ol. Shaw and Whiting,[3] who were actually in need of the acid (V), report that oxidation of the enyne alcohol with chromic acid (4 equiv. per mol. of alcohol) gives 69% of hept-*trans*-2-en-6-yn-1-al and 11% of hept-*trans*-2-en-6-ynoic acid. In our work a preponderance of acid (70%) over aldehyde (23%) was obtained when 5·6 equiv. of chromic acid were used, but by reducing the amount to 2·7 equiv. the yield of aldehyde was raised to 62%.

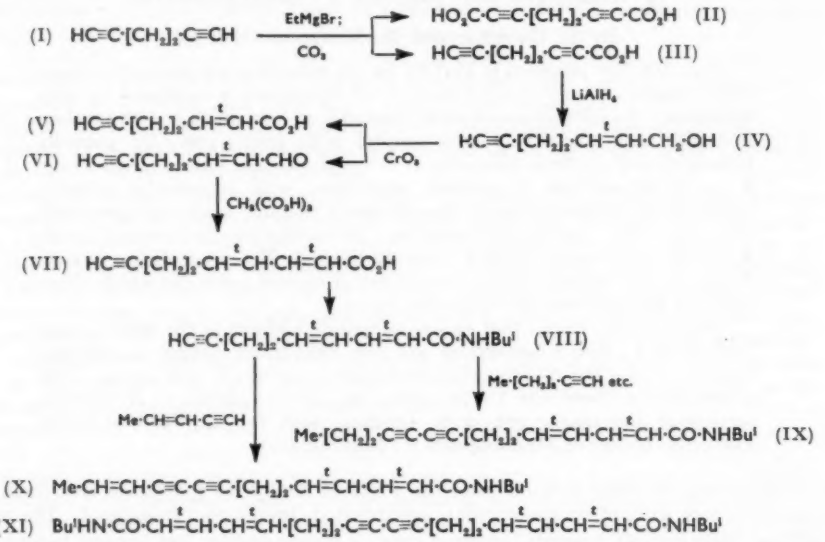
Doebner reaction between hept-*trans*-2-en-6-ynal and malonic acid gave nona-*trans*-2 : *trans*-4-dien-8-ynoic acid (VII) which was converted, *via* the acid chloride, into *N-iso*butylnona-*trans*-2 : *trans*-4-dien-8-ynamide (VIII) in excellent yield. Glaser oxidative coupling with pent-1-yne (3 mol.) gave the cross-coupled material (IX) and only small

* Part VIII, preceding paper.

[1] Crombie, *J.*, 1955, 999.
[2] Crombie and Manzoor-i-Khuda, *Chem. and Ind.*, 1956, 409.
[3] Shaw and Whiting, *J.*, 1954, 3217.

XUM

amounts of the symmetrical by-product (XI) were formed. Synthetic *N-iso*butyltetradeca-*trans*-2 : *trans*-4-diene-8 : 10-diynamide (IX) was a colourless solid which became pink in light and eventually deteriorated to an orange-red substance. It did not depress the



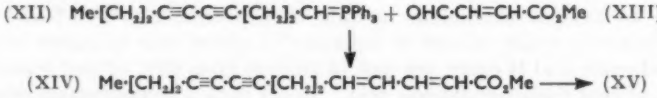
m. p. of natural anacyclin, and spectral data support the identity (Table 1 and p. 2774). When hydrogenated (2 mol.) over Lindlar catalyst, synthetic anacyclin gave a crystalline tetrahydro-derivative which, on the basis that such reductions give largely stereospecific

TABLE 1. *Natural and synthetic anacyclin.*

	M. p.	H_2 [b]	$\lambda_{max.}$ (mμ)	ε	Adduct,[c] m. p.
Natural anacyclin [a]	121°	5·8	259	33,500	193°
Synthetic anacyclin	121	6·1	258	34,000	193

[a] Crombie, Part IV. [b] Mols. of hydrogen absorbed over a platinum catalyst. [c] Adduct with maleic anhydride.

cis-addition of hydrogen to an acetylenic linkage, is formulated as *N-iso*butyltetradeca-*trans*-2 : *trans*-4 : *cis*-8 : *cis*-10-tetraenamide. Spectroscopic and other data are consistent with this formulation, and the tetraenamide is insecticidally active.



Almost simultaneously with the publication of our note,[2] Bohlmann and Inhoffen described a different synthesis.[4] This involved cross-coupling pent-1-yne with pent-4-ynol, conversion into the bromide, and then synthesis by the Wittig–Schöllkopf reaction [5] using the aldehyde (XIII) prepared by oxidation of crotonic ester with selenium dioxide. The final stages (XIV) ⟶ (XV) involved successive hydrolysis by alkali and reaction with thionyl chloride and then *iso*butylamine. It is not clear if *trans*-2 : *cis*-4 material was also formed in the Wittig–Schöllkopf reaction, and yields of purified product were not reported.

[4] Bohlmann and Inhoffen, *Chem. Ber.*, 1956, **89**, 1276.
[5] Wittig and Schöllkopf, *Chem. Ber.*, 1954, **87**, 1318.

TABLE 2. *Ultraviolet data for unsaturated amides and related substances.**

TABLE 2. *Ultraviolet data for unsaturated amides and related substances.**

Me·[CH$_2$]$_4$·CH=CH·CH=CH·CO$_2$H [a]	257 (28,500)
HC≡C·[CH$_2$]$_3$·CH=CH·CH=CH·CO$_2$H	257 (25,000)
Me·[CH$_2$]$_4$·CH=CH·CH=CH·CO·NHBu^t [a]	258 (29,500)
HC≡C·[CH$_2$]$_3$·CH=CH·CH=CH·CO·NHBu^t	258 (34,000)
(·C≡C·[CH$_2$]$_3$·CH=CH·CH=CH·CO·NHBu^t)$_2$	257 (71,500)
Me·[CH$_2$]$_3$·C≡C·C≡C·[CH$_2$]$_3$·CH=CH·CH=CH·CO$_2$H	257 (26,500)
Me·[CH$_2$]$_3$·C≡C·C≡C·[CH$_2$]$_3$·CH=CH·CH=CH·CO·NHBu^t	258 (34,000)
Me·[CH$_2$]$_4$·C≡C·C≡C·[CH$_2$]$_3$·CO$_2$H	226 (440); 240 (440); 252 (250)
Me·[CH$_2$]$_3$·C≡C·C≡C·[CH$_2$]$_3$·Me [b]	228 (440); 239·5 (390); 254 (240)
Me·CH=CH·C≡C·C≡C·[CH$_2$]$_2$·CH=CH·CH=CH·CO·NHBu^t	255 (44,500); 267 (52,000); 283 (28,000)
Me·CH=CH·C≡C·C≡C·[CH$_2$]$_2$·CH=CH·CH=CH·CO·NHBu^t	256 (35,000); 267 (43,000); 283 (19,000)
Me·[CH$_2$]$_3$·CH=CH·C≡C·C≡C·[CH$_2$]$_7$·CO$_2$Me [a]	229 (3000); 240 (6000); 253 (12,500); 267 (20,000); 283 (15,500)
Me·[CH$_2$]$_3$·C≡C·C≡C·CH=CH·CH$_2$·OH [d]	239·5 (7300); 252 (14,600); 266·5 (21,850); 282·5 (19,440)

* Wavelength in mμ; ε in parentheses.
[a] Part V. [b] Armitage *et al.*, *J.*, 1952, 1998. [c] Crombie and Jacklin, *J.*, 1957, 1632. [d] Bruun *et al.*, *Acta Chem. Scand.*, 1950, **4**, 850.

TABLE 3. *Ultraviolet data for maleic adducts.* †*

(XVII); R = Me·[CH$_2$]$_3$·C≡C·C≡C·[CH$_2$]$_2$·	240 (650); 254 (410)
(XVII); R = Me·CH=CH·C≡C·C≡C·[CH$_2$]$_2$·	239 (5500); 252 (13,200); 266 (19,400); 282 (15,000)
(XVII); R = Me·CH=CH·C≡C·C≡C·[CH$_2$]$_2$·	240 (4250); 253 (8500); 267 (12,950); 282 (10,700)

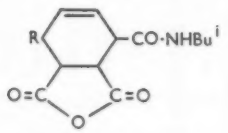
* Wavelength in mμ; ε in parentheses.
† (XVII), where R = Me or Me·[CH$_2$]$_4$·, show no high-intensity maxima in the usual range, but rising end-absorption ε ~ 2000 at 210 mμ. See Table 2 for comparative chromophores.

TABLE 4. *Infrared assignments (cm.$^{-1}$) for unsaturated* isobutylamides.‡

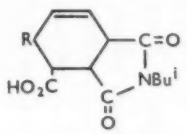
	NH		C≡C	C=O	CH=CH$_I$	CH=CH$_{II}$	Amide B	δ′ (CH=CH)$_2$
Me·[CH$_2$]$_4$·[CH=CH]$_2$·CO·NHBu^t [a]	3295	3075	—	1625	1654	1614	1550	994
HC≡C·[CH$_2$]$_3$·[CH=CH]$_2$·CO·NHBu^t	3247	3021	2119	1626	1653	1608	1538	996
[·C≡C·[CH$_2$]$_3$·[CH=CH]$_2$·CO·NHBu^t]$_2$	3263	3030	— [f]	1625	1655	1609	1540	997
Pr^n·[C≡C]$_2$·[CH$_2$]$_3$·[CH=CH]$_2$CO·NHBu^t	3248	3049	— [f]	1622	1653	1609	1540	1000
Me·CH=CH·[C≡C]$_2$·[CH$_2$]$_3$·[CH=CH]$_2$·CO·NHBu^t	3236	3040	2232	1621	1650	1612	1546	997
Me·CH=CH·[C≡C]$_2$·[CH$_2$]$_3$·[CH=CH]$_2$·CO·NHBu^t	3236	3040	2232	1623	1652	1608	1538	996
Pr^n·[CH=CH]$_2$·[CH$_2$]$_3$·[CH=CH]$_2$·CO·NHBu^t	3273	3049	—	1623	1659	1611	1538	1005
Bu^n·[CH=CH]$_2$·[CH$_2$]$_7$·CO·NHBu^t	3252	3049	—	1639	—	—	1554	1006

‡ Paraffin mull spectra. [a] Part V. [f] Acetylenic vibrations very weak or undetectable.

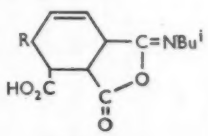
The best samples of anacyclin isolated from natural sources contain about 4% of a conjugated enediyne impurity, as judged by their ultraviolet spectra.[1] This second substance is likely to be closely related to anacyclin and a fair assumption is that the contaminant might be *N-iso*butyltetradeca-*trans*-2 : *trans*-4 : *trans*-12- or -*trans*-2 : *trans*-4 : *cis*-12-triene-8 : 10-diynamide (X). We have prepared both these compounds though it is not yet possible to say if either is the natural conjugated enediyne. For synthesis of compounds of this type, our approach is particularly useful as the flexibility of the final stage enables the standard unit (VIII) to be coupled with a variety of acetylenic hydrocarbons. Both pure *cis*- and pure *trans*-pent-2-en-4-yne [6] were oxidatively coupled with the amide (VIII) to give the two crystalline stereoisomers (X) mentioned above. Each absorbed 7 mols. of hydrogen over a catalyst to give *N-iso*butyltetradecanamide. Infrared spectra (see p. 2775) are in agreement with the allotted configurations; for, besides the usual strong absorption near 996 cm.$^{-1}$ due to the *trans-trans*-conjugated diene system, the *trans*-12-compound has a strong band at 948 cm.$^{-1}$ whilst the *cis*-12-compound has a strong band at 718 cm.$^{-1}$. These are characteristic of *trans*- and *cis*-enynes or -enediynes respectively. There is absorption near 948 cm.$^{-1}$ in the *cis*-12-amide and near 718 cm.$^{-1}$ in the *trans*-12-amide but this does not necessarily mean that partial stereomutation has occurred, for similar coincidences have been found in related pairs of geometrical isomers.[6]



(XVI)



(XVII)



(XVIII)

The ultraviolet spectra are the combined results of the absorption due to a *trans-trans*-dienamide and an enediyne chromophore. Table 2 makes it clear that the intensity contribution of a *cis*-enediyne is less than of the *trans*-isomer, and this is borne out by data for the maleic anhydride adducts (Table 3) in which the dienamide absorption is eliminated. In the infrared region, only the *trans*-enediyne adduct has, as expected, a band at 951 cm.$^{-1}$ and the *cis*-adduct has strong absorption at 722 cm.$^{-1}$.

The structure of maleic anhydride adducts of *N-iso*butyl-*trans*-2 : *trans*-4-dienamides is of interest. Although we have mentioned them earlier and used them in structural work, we have not assigned a structure to them. Bohlmann and Inhoffen [4] have recently given the maleic anhydride adduct from anacyclin the obvious structure (XVI; R = Pr·[C≡C]$_2$·[CH$_2$]$_2$·). Infrared data lead us to the view that this is incorrect; for, in a series of such adducts, no characteristic vibrations for NH, amide A (carbonyl), amide B, or the anhydride ring can be found. The usual positions for these can be found in Table 5 by reference to the maleic anhydride adducts of *N-iso*butyloctadeca-*trans*-9 : *trans*-11 : *trans*-13-trienamide and α- or β-sanshoöl (such adducts are "normal" as the triene system is remote from the carboxyamide function). Analysis shows that the maleic anhydride adducts of *N-iso*butyl-*trans*-2 : *trans*-4-dienamides must be isomeric with structure (XVI) and on catalytic hydrogenation they absorb 1 mol. of gas. Observations of the infrared spectrum near 2500 cm.$^{-1}$ (broad band) suggest that a free carboxylic acid group is present in the "abnormal" adducts.

Alternative formulations (XVII) and (XVIII) are possible, the former being more consistent with the infrared data. Like *N-iso*butylsuccinimide, prepared as a model substance, all the abnormal maleic anhydride adducts have a strong band near 1200 cm.$^{-1}$ and two others near 1760 and 1705 cm.$^{-1}$. Dr. Elvidge has told us that he and his co-workers have found a wide range of *N*-unsubstituted imides to have a strong band near 1190 and two near 1770 and 1695 cm.$^{-1}$. On this basis the bands near 1760 and 1705 cm.$^{-1}$

[6] Allan and Whiting, *J.*, 1953, 3314; Allan, Meakins, and Whiting, *J.*, 1955, 1874.

are associated with the imide structure and a third strong band near 1675 cm.$^{-1}$ is assigned to the carboxylic acid function in (XVII). For a normal saturated carboxylic acid group, the carbonyl stretching frequency is low (Bellamy [7] gives 1700—1725 cm.$^{-1}$). The maleic adduct from *N-iso*butylsorbamide was therefore esterified with diazomethane. In the ester, the band at 1672 cm.$^{-1}$ had disappeared and a new strong band at 1731 cm.$^{-1}$ appeared. This is near the normal position for an α-saturated ester (Bellamy [7] gives 1735—1750 cm.$^{-1}$). The bands associated with the imide group were at 1770, 1704, and 1202 cm.$^{-1}$. The assignments in Table 5 therefore seem reasonable.

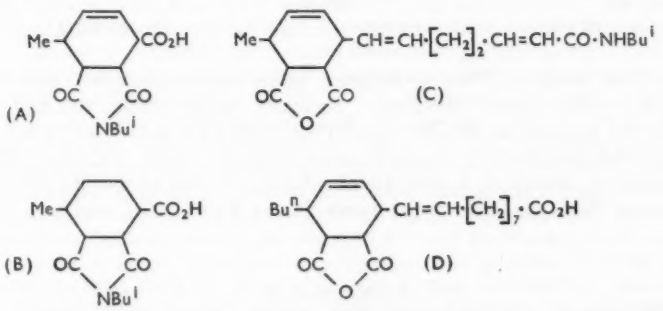
TABLE 5. *Infrared spectra (cm.$^{-1}$) of Diels–Alder adducts.* †*

	Imide Carbonyl Region			Carboxylic	Imide
Imides :					
Hexahydrophthalimide [a]	1786	—	1695	—	1189
Succinimide [a]	1770	—	1704	—	1190
*N-iso*Butylsuccinimide	1765	1739i	1706	—	1203
*N-iso*Butylmaleimide [b]	1757	1727i	1709	—	1196
(XVII); R = Me·$[CH_2]_4$·	1757	1724i	1709	1675	1198
(XVII); R = Pr^n·$[C{\equiv}C]_2$·$[CH_2]_2$·	1754	—	1707	1677	1198
(XVII); R = Me·$CH{=}^{t}CH$·$[C{\equiv}C]_2$·$[CH_2]_2$·	1754	1721i	1706	1678	1204
(XVII); R = Me·$CH{=}^{c}CH$·$[C{\equiv}C]_2$·$[CH_2]_2$·	1757	1724i	1709	1678	1200
(XIX)	1752	—	1709	1672	1198
(XX)	1757	1721i	1704	1667	1206
(A)	1767	1736		1692	1208
(XXI)	1751	—	1704	1669	1205
			1709i		
(B)	1767	1736	1709	1681	1211
			1701		

	NH	Anhydride	α-C=C	Amide	
Anhydrides :					
trans-2 : *cis*-6-(C) [c]	3295, 3125	1838, 1765	1669	1618	1543
trans-2 : *trans*-6-(C) [c,d]	3280, 3040	1842, 1768	1664	1618	1547
trans-9-(D) [d]	3260, 3050	1843, 1770	—	1645	1547

* Paraffin mull spectra. † The band near 1760 cm.$^{-1}$ in the imides is normally considerably weaker than the other tabulated bands.

[a] Elvidge and Bull, personal communication. [b] There are also bands at 1684, 1604, and 1588 cm.$^{-1}$. [c] Crombie and Tayler, Part VIII. [d] These may be mixtures of the two isomers derived from the two possible modes of addition to an all-*trans*-triene.



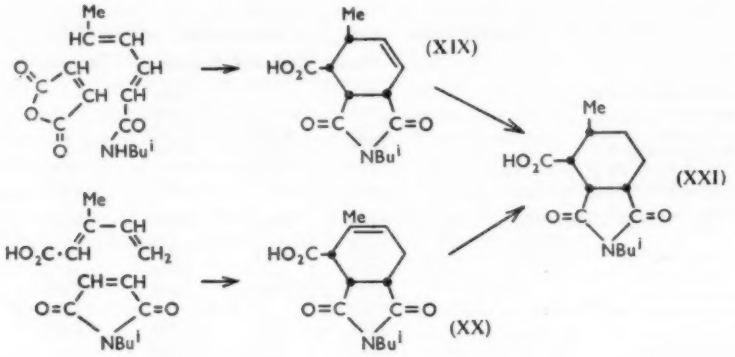
An attempt was then made to establish the structure of the " abnormal " adducts by synthesis in the following way. 3-Methylpenta-2 : 4-dienoic acid was prepared by modification of a method described by Heilbron *et al.*[8] which involves Reformatski reaction between methyl vinyl ketone and ethyl bromoacetate. A Diels–Alder reaction between 3-methylpenta-2 : 4-dienoic acid and *N-iso*butylmaleimide gave an adduct having spectroscopic data (Table 5) consistent with structure (XX). On catalytic hydrogenation in acidic

[7] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1954.
[8] Heilbron, Jones, Julia, and Weedon, *J.*, 1949, 1823.

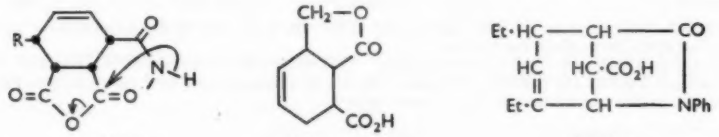
XUM

or neutral solution a saturated imide was formed which, on the basis of hindrance to the formation of a *trans*-methyl at the catalyst surface,[9] should be the all-*cis*-compound (XXI). This substance was equated by mixed m. p. with the product obtained when the maleic adduct of *N*-*iso*butylsorbamide was hydrogenated. The all-*cis*-formulation is based on Alder's generalisations : related systems have been examined from this point of view.[10]

Formation of the *N*-*iso*butylimide (XVII) is considered to occur through nucleophilic attack by the amide grouping at the carbon atom of the adjacent anhydride carbonyl grouping, either during the Diels–Alder reaction, or subsequently, as shown diagram-



matically in (XXII). Two other unexpected reactions of a diene with maleic anhydride in benzene bear comparison. First, penta-2 : 4-dienol (and related alcohols), when treated with this reagent at 20°, gives directly the lactol (XXIII).[11] In agreement with this



(XXII) (XXIII) (XXIV)

structure we find bands at 1754s (γ-lactone), 1698s (carboxylic acid), and 1653w cm.$^{-1}$ (double bond) in the infrared spectrum. Secondly, under reflux, the anil of 2-ethylhexenal (believed to react as Et·CH=CH·CEt=CH·NHPh) is said [12] to form 2 : 4-diethyl-7-oxo-6-phenyl-6-aza*bicyclo*[3 : 2 : 1]oct-3-ene-8-carboxylic acid (XXIV). Such intramolecular reactions, involving a substituent adjacent to the anhydride ring, may occur more commonly than has been appreciated during Diels–Alder reactions with maleic anhydride.

Experimental

Analyses and light-absorption measurements were carried out in the microanalytical (Miss J. Cuckney) and spectrographic (Mrs. I. Boston and Mr. R. L. Erskine) laboratories of this Department. The ultraviolet absorptions were determined in pure ethanol with a Unicam S.P. 500 instrument (I.B.), and the infrared absorptions with a Grubb-Parsons double-beam

[9] Linstead, Doering, Davis, Levine, and Whetstone, *J. Amer. Chem. Soc.*, 1942, **64**, 1985.
[10] Alder and Schumacher, *Annalen*, 1950, **571**, 87, 108, 122; Alder and Vogt, *ibid.*, p. 137; Alder and Vagt, *ibid.*, p. 153; Craig, *J. Amer. Chem. Soc.*, 1950, **72**, 1678.
[11] Heilbron, Jones, McCombie, and Weedon, *J.*, 1945, 84.
[12] Snyder, Hasbrouck, and Richardson, *J. Amer. Chem. Soc.*, 1939, **61**, 3558.

instrument (R.L.E.). Unless otherwise indicated, infrared data relate to pure films for liquids and paraffin mulls for solids. For further data see Tables.

Hepta-2 : 6-diynoic Acid (III).—A Grignard reagent was prepared from magnesium (15·65 g.) and ethyl bromide (72 g.) in dry tetrahydrofuran (150 ml.) and added dropwise with vigorous stirring to hexa-1 : 5-diyne (50 g.; prepared [13] in 64—67% yield) in tetrahydrofuran (200 ml.). The mixture was set aside (16 hr.) and washed into an autoclave with tetrahydrofuran (70 ml.). Solid carbon dioxide (2½ lb.) was added and the autoclave sealed and set aside (3 days). The product was then decomposed with water and 2N-sulphuric acid and thoroughly extracted with ether. After drying (Na_2SO_4), the extracts were evaporated and the solid product was triturated with cold benzene. Octa-2 : 6-diyndioic acid (15·5 g., 15%) was filtered off and had m. p. 190° after crystallisation. The filtrate was extracted with 2N-sodium hydroxide, and the alkaline extract acidified. Collection with ether, drying, and evaporation gave a solid which was distilled at 0·001 mm. (bath 110—135°). The distillate (26·5 g., 34%) was used directly for esterification; a specimen crystallised once from light petroleum (b. p. 40—60°) gave hepta-2 : 6-diynoic acid, m. p. 53—54°. On a smaller scale, with ethylmagnesium bromide [from magnesium (3·11 g.) and ethyl bromide (14 g.)] in tetrahydrofuran (50 ml.), and hexa-1 : 5-diyne (10 g.) in tetrahydrofuran (25 ml.), and procedure as above, octa-2 : 6-diynedioic acid (approx. 5%) and hepta-2 : 6-diynoic acid (53%; 47% after crystallisation to m. p. 52—53°) were isolated.

Hexa-1 : 5-diyne (40 g.) in tetrahydrofuran (75 ml.) was added slowly, with stirring, to a Grignard reagent prepared from magnesium (12·5 g.), ethyl bromide (56 g.), and tetrahydrofuran (250 ml.), and the mixture stirred (16 hr.) and then heated in nitrogen under reflux for 1 hr. Carboxylation and working up as above gave octa-2 : 6-diynedioic acid (24 g., 28%) and hepta-2 : 6-diynoic acid (7 g., 11%; 6 g. after crystallisation to m. p. 53°). Using this direction of addition, Shaw and Whiting [3] obtained octa-2 : 6-diynedioic acid, m. p. 189—190° (22%), and hepta-2 : 6-diynoic acid, m. p. 52·5—53·5° (18%).

Ethyl Hepta-2 : 6-diynoate.—Hepta-2 : 6-diynoic acid (26·5 g.) was added to benzene (31 ml.) containing ethanol (17 ml.) and concentrated sulphuric acid (1·8 ml.), and heated under reflux for 17 hr. in nitrogen. Water was added and the organic layer isolated with ether. Drying, evaporation, and distillation gave ethyl hepta-2 : 6-diynoate (30·5 g., 94%), b. p. 78°/0·6 mm., n_D^{21} 1·4693 [lit.,[3] b. p. 90° (bath-temp.)/1·5 mm., $n_D^{17\cdot5}$ 1·4718].

Methyl Hepta-2 : 6-diynoate.—Hepta-2 : 6-diynoic acid (4·0 g.) in dry ether (25 ml.) was treated at 0—5° with diazomethane in ether (added dropwise) until reaction appeared complete. Evaporation *in vacuo* and distillation gave the *methyl ester* (4·22 g., 96%), b. p. 82°/10 mm., n_D^{21} 1·4721 (Found: C, 70·75; H, 6·05. $C_8H_8O_2$ requires C, 70·55; H, 5·9%). Infrared bands at 3245s, 2153w, 2135w (C≡CH), 2244s (C≡C conj. with CO_2Me) and 1711s cm.$^{-1}$ (CO_2Me).

In another experiment the acid (17·5 g.) in ether was left in contact with excess of diazomethane for 2 days at 0°. Distillation gave the above methyl ester (14·8 g.), b. p. 84°/10 mm. The residue in the flask (6·5 g.) crystallised. Recrystallisations from ethanol and from toluene gave a *pyrazole*, m. p. 129° [Found: C, 60·55; H, 5·9; N, 15·55%; *M* (Rast), 203. $C_9H_{10}O_2N_2$ requires C, 60·65; H, 5·65; N, 15·7%; *M*, 178·2]. Ultraviolet max. at 224 mμ (ε 5800), and infrared bands at 3236m, 2118w (C≡CH), 1724s (CO_2Me), 1709s. The presence of a terminal ethynyl grouping shows that pyrazole formation must have occurred at the α-acetylenic linkage.

Hept-trans-2-en-6-yn-1-ol (IV).—Lithium aluminium hydride (25 g.) was suspended in dry ether (1 l.), and ethyl hepta-2 : 6-diynoate (19·2 g.) in dry ether (150 ml.) was slowly added to it and the mixture refluxed under nitrogen (3 hr.). Iced 8N-sulphuric acid was added and the product worked up to give *hept-trans-2-en-6-yn-1-ol* (12·7 g., 91%), b. p. 56°/0·5 mm., n_D^{21} 1·4745 (Found: C, 76·3; H, 9·25. $C_7H_{10}O$ requires C, 76·3; H, 9·15%). Infrared bands at 3333s (OH), 3246s, 2123m (C≡CH), 1675m, 969s (*trans*-CH=CH). Similar reduction of the methyl ester gave an 85% yield. Shaw and Whiting [3] give b. p. 106° (bath-temp.)/14 mm., n_D^{20} 1·4739, but could not obtain satisfactory analyses.

Hept-trans-2-en-6-yn-1-al (VI).—Hept-*trans*-2-en-6-yn-1-ol (6 g.) was dissolved in acetone (40 ml.), and a solution (20 ml.) of chromic acid (8N) [2·9 equiv. per mol. of alcohol] in 12N-sulphuric acid added slowly, and with stirring, the temperature being kept below 35°. The mixture was stirred for 2 hr. at 25° and set aside for 18 hr. at 0°. Brine was added, and the solution extracted thoroughly with ether. The ethereal extracts were themselves extracted with N-potassium hydroxide, and the acidic material (1%) was isolated. The neutral ethereal

[13] Raphael and Sondheimer, *J.*, 1950, 120.

solution was dried, evaporated, and distilled, to give hept-*trans*-2-en-6-yn-1-al (3·65 g., 62%), b. p. 76°/10 mm., $n_D^{22\cdot5}$ 1·4828.

Hept-2-en-6-yn-1-ol (19 g.) was dissolved in acetone (120 ml.), and a solution (120 ml.) of chromic acid (8N) [5·6 equiv. per mol. of alcohol] in 12N-sulphuric acid added slowly and with stirring, at 20—30°. After being stirred at 20° for 2 hr. and set aside for 18 hr., the product was worked up as above to give hept-2-en-6-yn-1-al (4·3 g., 23%) and hept-2-en-6-ynoic acid (15 g., 70%). Using 4 equivs. of chromic acid per mol. of alcohol, Shaw and Whiting obtained 69% of aldehyde and 11% of acid. Hept-*trans*-2-en-6-yn-1-al had infrared bands at 3240, 2262, 2210, 2126 (C≡CH), 2809, 2732, 1686 (C−H and C=O vibrations of α-unsaturated aldehyde), 1634 and 971 cm.$^{-1}$ (conj. *trans*-CH=CH).

Nona-trans-2 : trans-4-*dien*-8-*ynoic Acid* (VII).—Hept-*trans*-2-en-6-ynal (2·35 g.) was dissolved in pyridine (5·5 ml.), and malonic acid (3·7 g.) added. The mixture was set aside for 3 days (the malonic acid dissolved in a few hours) and then heated on the steam-bath for 1 hr. and poured into 2N-hydrochloric acid. The product was extracted with ether, and the ethereal solution extracted with 2N-sodium hydroxide. Acidification and isolation with ether gave *nona*-trans-2 : trans-4-*dien*-8-*ynoic acid* which, when distilled at 118°/0·35 mm., solidified (2·3 g., 72%). Crystallisation from light petroleum (b. p. 40—60°) gave the acid as plates (1·3 g., 41%), m. p. 100—101° (Found : C, 71·8; H, 6·9. $C_9H_{10}O_2$ requires C, 72·0; H, 6·7%). Ultraviolet max. 257 mμ (ε 25,500); infrared max. at 3236m, 2117mw (C≡CH), 1685s (conj. CO_2H), 1631m, 1613m, 998m (conj. *trans-trans*-diene). For comparative data see Part VII.

Nona-trans-2 : trans-4-*dien*-8-*ynoyl Chloride*.—The acid (1·00 g.) was treated with thionyl chloride (1·5 g.), set aside (3 hr.), and then heated at 100° (10 min.). The *acid chloride* (0·98 g., 88%) distilled at 68—76°/1·5 mm. (Found : C, 63·8; H, 5·45. C_9H_9OCl requires C, 64·1; H, 5·4%).

N-iso*Butylnona*-trans-2 : trans-4-*dien*-8-*ynamide* (VIII).—The acid chloride (0·92 g.) was added, dropwise and with shaking, to *iso*butylamine (1·2 g.) in dry ether (50 ml.), and the product was set aside for 2 hr. and then washed with water, 2N-hydrochloric acid, sodium hydrogen carbonate solution, and water. After drying and evaporation, the residue was crystallised from light petroleum (b. p. 60—80°). The N-iso*butylamide* (0·78 g., 69%) had m. p. 91° (Found : C, 75·85; H, 9·4; N, 6·8. $C_{13}H_{19}ON$ requires C, 76·05; H, 9·35; N, 6·8%). Ultraviolet max. 258 mμ (ε 34,000).

N-iso*Butyltetradeca*-trans-2 : trans-4-*diene*-8 : 10-*diynamide* (*Anacyclin*) (IX).—*N-iso*Butylnona-*trans*-2 : *trans*-4-dien-8-ynamide (500 mg.) and pent-1-yne (550 mg.) were dissolved in methanol (10 ml.), and a solution of cuprous chloride (1·2 g.) and ammonium chloride (2·5 g.) in 0·08N-hydrochloric acid (10 ml.) added. The mixture was shaken in oxygen for 4½ hr. (no further gas absorption after 2½ hr.). 2N-Hydrochloric acid was added and the solution extracted with ether containing a little chloroform. The extracts were dried and evaporated and the residue boiled with light petroleum (b. p. 60—80°) containing a little chloroform and filtered hot. N-iso*Butyltetradeca*-trans-2 : trans-4-*diene*-8 : 10-*diynamide* (344 mg., 52%) crystallised from the filtrate and, recrystallised from light petroleum (b. p. 60—80°), had m. p. 121° (Found : C, 79·15; H, 9·25. $C_{18}H_{25}ON$ requires C, 79·65; H, 9·3%). When admixed, it did not depress the m. p. of natural anacyclin, m. p. 119—120°. The amide became bright pink on exposure to light. On microhydrogenation (6·1H_2 absorbed), *N-iso*butyltetradecanamide, m. p. and mixed m. p. 65°, was obtained. *all*-trans-*Di*-(N-iso*butyl*)*octadeca*-2 : 4 : 14 : 16-*tetraene*-8 : 10-*diyne*-1 : 18-*diamide*, insoluble in light petroleum containing a little chloroform (see above; 71 mg., 4%), crystallised from chloroform containing a little light petroleum and had m. p. 245—246° (decomp.), becoming rose-pink at about 100° [Found : C, 76·15; H, 8·7%; *M* (Rast), 429. $C_{26}H_{36}O_2N_2$ requires C, 76·45; H, 8·9%; *M*, 409]. See Tables for spectral data. Natural and synthetic anacyclin had infrared max. at 3248, 3031, 2717, 2156, 1986, 1747, 1653, 1622, 1608, 1537, 1453, 1373, 1350, 1336, 1302, 1294, 1258, 1207, 1167, 1158, 1139, 1129, 1088, 1075, 1062, 1035, 1000, 944, 925, 898, 872, 817, 734, 723 cm.$^{-1}$.

Anacyclin–Maleic Anhydride Adduct.—Synthetic anacyclin (80 mg.) was heated in a sealed tube with maleic anhydride (30 mg.) in benzene (0·5 ml.) for 16 hr. at 100°. The solid which crystallised (80 mg.) was decolorised with charcoal and recrystallised from benzene, to give the *adduct* (35 mg.), m. p. 193° decomp. (Found : C, 71·25; H, 7·5. $C_{22}H_{27}O_4N$ requires C, 71·5; H, 7·35%).

Tetradeca-trans-2 : trans-4-*diene*-8 : 10-*diynoic Acid*.—Nona-*trans*-2 : *trans*-4-dien-8-ynoic acid (140 mg.) and pent-1-yne (210 mg.), dissolved in methanol (4 ml.), were added to a solution

of cuprous chloride (0·4 g.) and ammonium chloride (1 g.) in 0·08N-hydrochloric acid (4 ml.). Oxidative coupling (3½ hr.), as above, gave *tetradeca*-trans-2 : trans-4-*diene*-8 : 10-*diynoic acid* (160 mg., 80%), m. p. 148—152°, raised by crystallisation from a mixture of light petroleum (b. p. 60—80°) and ether to 154—155° (Found : C, 77·6; H, 7·45. $C_{14}H_{16}O_2$ requires C, 77·75; H, 7·45%). Infrared max. (paraffin mull) : 2150vw (diyne), 1688s, 1677s (CO_2H), 1635m, 1614m, 1003m (conj. *trans-trans*-diene α to carboxyl). The acid was converted into the acid chloride with thionyl chloride and treated with *iso*butylamine, to give *N-iso*butyltetradeca-*trans*-2 : *trans*-4-diene-8 : 10-diynamide, m. p. 121°, equated with natural anacyclin by the infrared spectrum. Bohlmann and Inhoffen [4] report the acid to have m. p. 58°.

Pent-trans-3- *and Pent*-cis-3-*enyne*.—The *cis–trans*-hydrocarbon mixture was prepared and separated by fractional distillation through a Stedman column according to Allan and Whiting's directions.[6] Pent-*cis*-3-enyne had b. p. 45·0—45·1°, n_D^{27} 1·4278, and the *trans*-stereoisomer, b. p. 52·1—52·2°, $n_D^{21\cdot5}$ 1·4352 [lit. : [6] *cis*, b. p. 44·5—44·6°, n_D^{20} 1·4330 (n_D^{27} 1·4285 using temp. coeff. 0·00064); *trans*, b. p. 52·0—52·2°, n_D^{20} 1·4368 ($n_D^{21\cdot5}$ 1·4358 using temp. coeff. 0·00067)]. The infrared spectra corresponded with the recorded data.[6]

N-iso*Butyltetradeca*-trans-2 : trans-4 : trans-12-*triene*-8 : 10-*diynamide* (X).—*N-iso*Butylnona-*trans*-2 : *trans*-4-dien-8-ynamide (600 mg.) and pent-*trans*-3-enyne (700 mg.) in methanol (11 ml.) were added to a solution of cuprous chloride (1·1 g.) and ammonium chloride (2·75 g.) in 0·08N-hydrochloric acid (11 ml.) and oxidatively coupled (4 hr.). Working up as usual gave N-iso-*butyltetradeca*-trans-2 : trans-4 : trans-12-*triene*-8 : 10-*diynamide* (450 mg., 61%) which when crystallised from light petroleum (b. p. 60—80°)–chloroform had m. p. 150·5° (Found : C, 80·3; H, 8·6. $C_{18}H_{23}ON$ requires C, 80·25; H, 8·6%). The product was not very photosensitive though it became faintly rose-pink on prolonged exposure to sunlight. It had infrared max. at 3236, 3040, 2874, 2703, 2398, 2232, 1859, 1725, 1650, 1621, 1612, 1546, 1452, 1374, 1364, 1351, 1342, 1300, 1264, 1209, 1164, 1155, 1147, 1126, 1108, 1082, 1062, 1030, 997, 948, 909, 866, 818, 736, 724, 676 cm.$^{-1}$. On microhydrogenation (6·75 H_2 absorbed), a tetradecahydro derivative, m. p. 65°, was obtained, undepressed on admixture with *N-iso*butyltetradecanamide. Symmetrically coupled material (XI) (50 mg.), m. p. 244—246°, was also isolated. A *maleic anhydride adduct* was prepared by heating the trienediynamide (100 mg.) with maleic anhydride (40 mg.) in benzene (0·8 ml.) in a sealed tube for 18 hr. and, recrystallised from benzene (charcoal), had m. p. 186—187° (Found : N, 3·9. $C_{22}H_{25}O_4N$ requires N, 3·8%).

N-iso*Butyltetradeca*-trans-2 : trans-4 : cis-12-*triene*-8 : 10-*diynamide* (X).—*N-iso*Butylnona-*trans*-2 : *trans*-4-dien-8-ynamide (550 mg.) and pent-*cis*-3-enyne (700 mg.) in methanol (11 ml.) were added to a solution of cuprous chloride (1·1 g.) and ammonium chloride (2·75 g.) in 0·08N-hydrochloric acid (11 ml.), and oxidatively coupled in the usual way, to give N-iso*butyltetradeca*-trans-2 : trans-4 : cis-12-*triene*-8 : 10-*diynamide* (354 mg., 52%) which, after crystallisation from light petroleum (b. p. 60—80°), had m. p. 100—101° (Found : C, 80·05; H, 8·65%). This had infrared max. at 3236, 3040, 2833, 2703, 2232, 1873, 1745, 1720, 1652, 1623, 1608, 1538, 1460, 1399, 1376, 1364, 1349, 1330, 1304, 1259, 1206, 1166, 1158, 1136, 1128, 1077, 1062, 1032, 996, 944, 924, 907, 871, 816, 769, 718 cm.$^{-1}$. The white product rapidly became dull pink in light. On microhydrogenation (6·7 H_2 absorbed), *N-iso*butyltetradecanamide, m. p. and mixed m. p. 65°, was isolated. Symmetrically coupled material (XI) (50 mg.), m. p. 244—246°, was also isolated. The *maleic anhydride adduct*, prepared as above, had m. p. 186—187° (Found : C, 71·5; H, 6·95. $C_{22}H_{25}O_4N$ requires C, 71·9; H, 6·85%). The infrared spectrum was different from that of the isomer containing a *trans*-12-linkage. For spectroscopic data see Tables.

N-iso*Butyltetradeca*-trans-2 : trans-4 : cis-8 : cis-10-*tetraenamide*.—Synthetic anacyclin (150 mg.) was hydrogenated in ethyl acetate (7 ml.), Lindlar catalyst deactivated with a drop of quinoline being used. When 1·95 mol. of hydrogen had been absorbed, the hydrogenation was discontinued and the catalyst filtered off. The filtrate was evaporated *in vacuo* at 20°, dissolved in ether, and washed with 2N-sulphuric acid and then water. The ethereal solution was dried (Na_2SO_4) and concentrated *in vacuo*. Light petroleum (b. p. 40—60°) was added, precipitating an oil. The supernatant layer was decanted and, on being set aside at 0°, deposited crystals : after recrystallisation in a similar manner the *tetraene-amide* (30 mg.) had m. p. 100—101° (Found : C, 78·75; H, 10·3. $C_{18}H_{29}ON$ requires C, 78·5; H, 10·6%). Microhydrogenation 3·9 H_2. Ultraviolet max. at 256 mμ (ε 34,000). The usual amide and diene bands were present in the infrared spectrum. The *tetraene-amide* was a sialogogue and was found [by Dr. M. Elliott and Mr. P. Needham (Rothamsted Experimental Station)] to be insecticidally active against mustard beetles.

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Maleic Anhydride Adduct of N-iso*Butylsorbamide*.—*N-iso*Butylsorbamide (5 g.) and maleic anhydride (2·7 g.) in benzene (40 ml.) were heated under reflux for 16 hr. After cooling, the *adduct* (XIX) (6 g.), m. p. 183—184° (unchanged by four crystallisations from benzene), was filtered off (Found: C, 63·35; H, 7·35. $C_{14}H_{19}O_4N$ requires C, 63·35; H, 7·2%). Microhydrogenation 1·04 H_2. Ultraviolet absorption: no high-intensity max. >210 mμ; ε at 210 and 280 mμ, 2100 and 75 respectively. The *dihydro-adduct* (XXI), crystallised from anhydrous benzene, had m. p. 168—169°, somewhat dependent on rate of heating (Found: C, 62·55; H, 7·5. $C_{14}H_{21}O_4N$ requires C, 62·9; H, 7·9%). It was prepared by hydrogenation in ethyl propionate at palladium–carbon.

The adduct, m. p. 183—184°, was converted into the *methyl ester*, a viscous liquid, b. p. 160°/0·5 mm., by treatment with ethereal diazomethane (Found: C, 64·35; H, 7·5. $C_{15}H_{21}O_4N$ requires C, 64·5; H, 7·6%).

3-*Methylpenta*-2: 4-*dienoic Acid*.—A Reformatski reaction was carried out in the usual way between zinc wool (25 g.) activated with mercuric chloride (0·2 g.) and covered with benzene (300 ml.), methyl vinyl ketone (27 g.), and ethyl bromoacetate (60 g.) in benzene (150 ml.). When reaction was complete, the mixture was heated under reflux for 2 hr., cooled, and treated with acetic acid (90 g.) in water (1·8 l.). The benzene layer was separated, washed until free from acid, dried, evaporated, and distilled, to give crude hydroxy-ester, b. p. 57—66°/4·5 mm. (16·2 g.), n_D^{20} 1·4366—1·4372. There was no ultraviolet absorption ($E_{1\,cm.}^{1\%} < 20$ at wavelengths >225 mμ). Infrared bands were at 3485 (OH), 1644, 995, 924 cm.$^{-1}$ (vinyl).

The hydroxy-ester (5·0 g.) was heated in nitrogen under reflux with phosphorus oxychloride (6·0 g.) in benzene (30 ml.) for 30 min. After being cooled and washed with water (3 × 50 ml.) the benzene solution was dried (Na_2SO_4), evaporated, and distilled, to give crude ester (3·2 g.), b. p. 46—75°/2 mm., n_D^{27} 1·4698—1·4715. Light absorption max. 250 mμ (ε 15,500). Infrared bands at 1710 (α-unsatd. ester), 1626 and 1600 (conj. diene), 991 and 928 cm.$^{-1}$ (conj. vinyl).

Crude diene ester (9·8 g.) was hydrolysed in nitrogen with potassium hydroxide (8·5 g.) in refluxing methanol (160 ml.) and worked up in the usual way, to give 3-methylpenta-2: 4-dienoic acid (2·7 g.), b. p. 88—100°/3—5 mm., n_D^{22} 1·5156 (Found: C, 64·35; H, 7·5. Calc. for $C_6H_8O_2$: C, 64·25; H, 7·2%). Light absorption max. 250 mμ (ε 18,500). Infrared bands at 1689 (α-unsatd. acid), 1639, 1627, and 1605, 1592 (conj. diene: the usual doublet seems to be split into four bands), 991, and 926 cm.$^{-1}$ (conj. vinyl). The *S*-benzylthiuronium salt had m. p. 161° (Found: C, 60·45; H, 6·55. Calc. for: $C_{14}H_{18}O_2N_2S$: C, 60·4; H, 6·5%). Heilbron and his collaborators [8] give b. p. 60°/0·05 mm., n_D^{22} 1·5186, light absorption max. 249 mμ (ε 20,500), *S*-benzylthiuronium salt of m. p. 162°.

N-iso*Butylmaleimide*.—Maleic anhydride (12·5 g.) was dissolved in dry benzene (20 ml.), and *N-iso*butylamine (15 g.) added. The mixture was heated under reflux for 30 min. with exclusion of moisture. After distillation of the solvent, water was added and the mixture filtered and washed with water. The solid product was purified by dissolution in sodium carbonate solution and, after extraction with ether, reprecipitated with acid and filtered off. The *half* iso*butylamide* (12·8 g.) was washed with water and dried *in vacuo*. It crystallised from benzene–light petroleum (b. p. 40—60°) in plates, m. p. 99—100° (Found: C, 56·1; H, 7·6%; equiv., 164. $C_8H_{13}O_3N$ requires C, 56·1; H, 7·65%; equiv., 171). There were infrared bands at 3185, 3040, 1706, 1637, 1589, and 1517 cm.$^{-1}$.

This amide (7·5 g.) was heated from 180° to 220° (bath temp.) at 760 mm. in a stream of nitrogen and then distilled under reduced pressure. N-iso*Butylmaleimide* (1·5 g.), m. p. 47—48°, was obtained in transparent crystals (Found: C, 62·45; H, 7·15. $C_8H_{11}O_2N$ requires C, 62·7; H, 7·25%). Microhydrogenation 1·0 H_2.

*N-iso*Butylsuccinimide, prepared by refluxing together *N-iso*butylamine and succinic anhydride, had m. p. 28° when crystallised from light petroleum (b. p. 40—80°).

N-iso*Butylmaleimide Adduct of* 3-*Methylpenta*-2: 4-*dienoic Acid*.—*N-iso*Butylmaleimide (0·35 g.) and 3-methylpenta-2: 4-dienoic acid (0·26 g.) were heated together in a sealed tube in benzene (1·7 ml.) at 100° for 16 hr. The *adduct* (XX) (0·3 g.) was recrystallised from benzene to m. p. 189—190° (Found: C, 63·2; H, 7·2. $C_{14}H_{19}O_4N$ requires C, 63·4; H, 7·2%). Microhydrogenation 0·97 H_2.

The *dihydro-adduct* (XXI) was prepared by hydrogenating the adduct (XX) in ethyl acetate over Adams platinum catalyst. Even when crystallised five times from benzene, the substance separated in poorer crystalline form (m. p. 168—170°: somewhat dependent on rate of heating) than the hydrogenated adduct prepared from maleic anhydride and *N-iso*butylsorbamide,

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though its m. p. was not depressed by the latter (Found: C, 63·05; H, 7·95. $C_{14}H_{21}O_4N$ requires C, 62·9; H, 7·9%). The infrared spectra of the two substances were closely similar though there were small variations at longer wavelengths, suggesting impurity in one or both samples. A second specimen of the dihydro-adduct was prepared by hydrogenation over Adams catalyst in glacial acetic acid. Filtration and evaporation left a chalky solid; this was extracted with ether, and light petroleum (b. p. 40—60°) added, and the solution allowed to crystallise at 0°, giving a small yield of the dihydro-adduct. This crystallised in needles, m. p. 168° undepressed by, and similar in form to, the material derived from *N-iso*butylsorbamide.

Maleic Anhydride Adduct of N-iso*Butyl-β-elæostearamide.*—*N-iso*Butyl-β-elæostearamide, prepared in the usual way, had m. p. 79—80° (Found: C, 79·0; H, 11·8. Calc. for $C_{22}H_{39}ON$: C, 79·2; H, 11·8%). Ultraviolet max. 258 (41,900), 268 (58,400), and 278 mμ (43,400). Jacobson [14] gives m. p. 78—79°. The maleic anhydride adduct, prepared from amide (200 mg.) and anhydride (57 mg.) in dry benzene (0·8 ml.) by heating at 100° for 16 hr., was an oil which eventually crystallised from ether–light petroleum (b. p. 30—40°) when cooled in solid carbon dioxide–ethanol. It had m. p. 46—49° (unsharp) and was difficult to purify completely. It may contain the products of addition to both the 9 : 11- and the 11 : 13-diene linkage.

N-iso*Butylmaleimide Adduct of Sorbic Acid.*—Prepared in the usual way from imide (0·34 g.) and acid (0·26 g.) in benzene (2·5 ml.), the *adduct* (0·27 g.) formed needles, m. p. 156·5—157° from benzene–light petroleum (b. p. 60—80°) (Found: C, 63·3; H, 7·35. $C_{14}H_{19}O_4N$ requires C, 63·4; H, 7·2%). When hydrogenated in ethyl acetate at Adams catalyst, a *dihydro-derivative* was isolated which, crystallised from benzene–ether–light petroleum (b. p. 40—60°), had m. p. 135—136° (Found: C, 62·7; H, 8·05. $C_{14}H_{21}O_4N$ requires C, 62·9; H, 7·95%).

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[14] Jacobson, *J. Amer. Chem. Soc.*, 1952, **74**, 3423.

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535. *Properties of Periodate-oxidised Polysaccharides. Part VI.* The Mucilage from* Dilsea edulis.

By Vincent C. Barry and Joan E. McCormick.

The mucilage extracted by dilute hydrochloric acid from the red alga, *Dilsea edulis*, has been shown to yield, on acid hydrolysis, D-galactose, xylose, glucurone, sulphuric acid, and traces of 3 : 6-anhydro-D-galactose and hydroxymethylfurfuraldehyde. By successive applications of the method of periodate oxidation followed by phenylhydrazine degradation results have been obtained on the basis of which the structures of the mucilage and its degradation products are discussed.

In a previous report [1] Barry and Dillon suggested that the main structural unit of this mucilage was a repeating unit of five D-galactopyranose residues, the first four of which were linked 1 : 3, while the fifth, which was linked 1 : 6, also carried a sulphuric acid residue on $C_{(4)}$. This suggestion was based on the results of periodate oxidation and on the difficulty of removing the sulphuric acid by alkaline hydrolysis. Subsequently, Dillon and McKenna [2] described acetylated and methylated derivatives of the mucilage and also showed that a uronic acid was present to the extent of about 10%. The uronic acid appeared to be present in the lactone form since determinations of combined sulphate in the mucilage by titration and by gravimetric methods gave approximately the same

* Part V, *J.*, 1955, 222.

[1] Barry and Dillon, *Proc. Roy. Irish Acad.*, 1945, **50**, *B*, 349.
[2] Dillon and McKenna, *ibid.*, 1950, **53**, *B*, 45.

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result. From a study of the methylated sugars resulting from the hydrolysis of the methylated mucilage these authors agreed that galactose was the main sugar present and that it was mostly linked 1 : 3. They did not, however, confirm the presence of 1 : 6-glycosidic linkages since they failed to isolate 2 : 3 : 4-tri-*O*-methylgalactose from the hydrolytic products of a methylated, sulphur-free, though degraded galactan.

The present findings confirm the presence of 10% of a uronic acid which has been identified as glucurone and reveal new constituents, xylose (*ca.* 7%) and 3 : 6-anhydro-D-galactose (trace). The mucilage appears to have a highly ramified structure in which the D-galactopyranose is linked, for the most part, 1 : 3. The other constituents are present in branches which are removed by degradation. These branches also contain galactose units linked 1 : 3 and 1 : 4. Some of the galactose units are esterified with sulphuric acid at $C_{(6)}$ and these appear to be present, mainly, in the outer parts of the macromolecule.

Acid hydrolysis of the mucilage was shown by chromatographic examination to yield, in addition to galactose and sulphuric acid, small amounts of xylose (*ca.* 7%) and glucurone (estimated as 10·0%) and traces of 3 : 6-anhydro-D-galactose and hydroxymethylfurfuraldehyde. The presence of the last compound together with 3 : 6-anhydrogalactose is not unexpected (cf. O'Neill [3]) and it has been shown to be formed from the anhydro-sugar under the conditions of hydrolysis. Examination of the behaviour of D-glucurone under these conditions eliminated the possibility that such treatment could have produced from the lactone the amount of xylose present in the hydrolysate.

The neutralised hydrolysate gave a mixture of osazones which was shown by paper chromatography to contain galactosazone, xylosazone, and, surprisingly, a substantial amount of 3 : 6-anhydro-D-galactosazone. The identity of the last was confirmed after isolation from an alumina column. The increase in the proportion of the anhydro-sugar, after treatment with phenylhydrazine, was thought to be due to elimination of combined sulphuric acid from barium galactose 3(or 6)-sulphate remaining in the hydrolysate. Configurational considerations rule out such an elimination if the sulphate groups are located at $C_{(2)}$ or $C_{(4)}$ of galactose residues (see Peat [4] and Percival [5] for reviews on anhydro-sugars and carbohydrate sulphates respectively). Subsequent experiments showed that barium galactose 6-sulphate on treatment for osazone formation is converted in part into 3 : 6-anhydrogalactosazone. Similar treatment of galactose failed to yield the anhydro-sugar. The behaviour of 3- and 6-sulphated sugars towards 0·5N-sulphuric acid at 90° is such that only in the case of the latter is there unhydrolysed sulphate remaining after 8 hr. Since combined sulphate was found in the mucilage hydrolysate, the indications are that the sulphate groups in the polysaccharide are located at $C_{(6)}$ of galactose residues.

Oxidation of the mucilage with sodium periodate, as described by Barry and Dillon,[1] yielded a product which, after acid hydrolysis, was shown chromatographically to contain galactose, xylose, and uronic acid. When a portion of the product was condensed with *iso*nicotinhydrazide (cf. Part III [6]) the nitrogen content of the material formed indicated that 31·5% of the sugar units present in the mucilage have α-glycol groupings. The oxidised mucilage was degraded by phenylhydrazine in acetic acid solution as described in Part IV.[7] Glyoxal and erythrose were isolated as osazones, and paper chromatography indicated the presence also of galactosazone and xylosazone. In addition, a polysaccharide material was recovered which had a higher sulphur content than the original mucilage and which was shown, after acid hydrolysis, to consist virtually of galactose. This material was in turn oxidised and degraded, yielding a small amount of glyoxalbisphenylhydrazone together with a polysaccharide substance having a lower sulphur content. A third, similar treatment gave material, still polysaccharide in character, in which the sulphur

[3] O'Neill, *J. Amer. Chem. Soc.*, 1955, **77**, 2837.
[4] Peat, *Adv. Carbohydrate Chem.*, 1946, **2**, 37.
[5] Percival, *Quart. Rev.*, 1949, **3**, 369.
[6] Barry, McCormick, and Mitchell, *J.*, 1954, 3692.
[7] Barry and Mitchell, *J.*, 1954, 4020.

content was further reduced. In view of the small amount of material remaining and its very high ash content, a fourth oxidation and degradation were not attempted. Purification of the degradation products could not be effected by dialysis as all the organic material passed through the membrane (cf. Barry and Dillon [1]).

We are here attempting to throw light on the structure of a complex polysaccharide without having recourse to the classical methods of methylation. The persistence after three periodate oxidations and phenylhydrazine degradations of a material, polysaccharide in character and containing galactose as the sole sugar present, indicates that the mucilage contains a back-bone or core of 1 : 3-linked galactopyranose units. The once degraded material consists virtually of galactose and has a sulphur content of 5·9%. Degradation reduces this to 3·8% and another oxidation and phenylhydrazine treatment brings about a further reduction to 2·4%. Reasons have already been given for assigning the sulphate group to $C_{(6)}$ of galactose units and the reductions in sulphur content can be explained by assuming that the core of 1 : 3-linked galactose units is flanked by 6-sulphated 1 : 3-linked residues which are removed stepwise by oxidation followed by degradation. This idea is illustrated by the structural repeating units (requiring S, 5·2, 4·0, and 2·3% respectively) put forward for the three degradation products (Figs. 1—3). It should be emphasised that the formulæ (Figs. 1—5) are designed merely to explain the results obtained, and are not advanced as firm structures for the mucilage and its degradation products (they are intended, partly, to be an aid in following the present discussion). The once oxidised mucilage contains xylose and glucurone. The xylose is therefore linked 1 : 3 and the glucurone, as a 6 ⟶ 3-lactone, is invulnerable to periodate. The degradation of this oxidised material removes all the glucurone and all but a trace of the pentose and these are probably present in peripheral side-chains. Further, the isolation of glyoxalbisphenylhydrazone and erythrosazone from the degradation products confirms previous assertions [1,2] that some of the galactopyranose residues are linked 1 : 4 because, of the constituents of the mucilage, only galactose can yield erythrosazone on periodate oxidation and degradation. The xylose in the side-chains is visualised as consisting of individual units joined on either side to periodate-vulnerable galactopyranose. The evidence for this is the presence of xylosazone among the degradation products, our experience being that phenylhydrazine only cleaves linkages contiguous to carbonyl groups and then only when cleavage will result in osazone formation. Similar considerations point to the presence in the side-chains of single 1 : 3-linked galactose residues attached on each side to periodate-vulnerable sugar units. The above conclusions, together with the approximate, relative proportions of the constituent sugars in the original material, are taken into account in the proposed structure of the outer side-chains, represented in Fig. 4, four of which must be associated

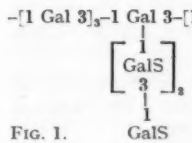

FIG. 1.

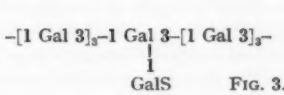

FIG. 3.

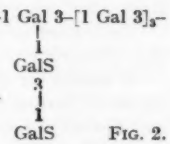

FIG. 2.

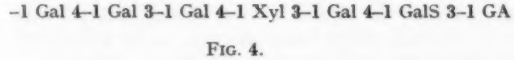

FIG. 4.

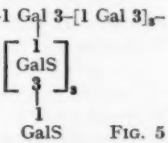

FIG. 5

(Gal = D-galactopyranose; GalS = D-galactopyranose sulphated at $C_{(6)}$; Xyl = xylose; GA = Glucurone.)

in the mucilage with each repeating unit of seven galactose and four sulphated galactose residues (Fig. 5). We have no information regarding the point of attachment of these

side-chains. However they are joined, oxidation followed by phenylhydrazine treatment will result in the formation of the once degraded material whose structure is given in Fig. 1. We have placed the glucurone as a terminal unit in the side-chain for the following reasons: Galactopyranose residues in this position would be oxidised by periodate and would yield glycerosazone on degradation. Again, the fact of the small amount (*ca.* 7%) of xylose in the mucilage together with the evidence of the presence of xylosazone in the products obtained after the first degradation make it unlikely that the outer side-chains are terminated by xylose residues. It is possible that some of the side-chains are terminated by 3 : 6-anhydrogalactose as this would also be invulnerable to periodate. The amount of this present is, however, too small to be considered as structurally significant.

Experimental

The mucilage was isolated from fronds of *Dilsea edulis* by Barry and Dillon's method [1] as a white, fibrous material. It was dissolved in water and precipitated by the addition of ethanol, then further purified by dialysis in 2% hydrochloric acid against distilled water. The product was a white, granular powder, $[\alpha]_D^{20} + 65{\cdot}7°$ (*c* 0·35 in H_2O) (Found: ash, 14·7; uronic anhydride, estimated by the method of Dickson, Otterson, and Link,[8] 10·0%).

The sulphur content of polysaccharide material was calculated from gravimetric estimations of barium sulphate derived from the material and from its ash, the assumption being made that the sulphate present in the ash was entirely inorganic in origin.

In the paper chromatography, the sugar mixtures were separated by elution with butan-1-ol–pyridine–water–benzene (5 : 3 : 3 : 1 v/v; top layer) [9] (*a*) or ethyl methyl ketone–acetic acid–water (6 : 1 : 1 v/v) [10] (*b*), and the osazone mixtures with benzene–95% ethanol (9 : 1 v/v) [7] (*c*). The sugars were located by spraying the paper with a solution of aniline hydrogen phthalate [11] or *p*-anisidine hydrochloride,[12] and the osazones by viewing the paper in ultra-violet light.

Aqueous solutions were concentrated at 40° under reduced pressure. Brockmann-standardised Merck alumina was used throughout for chromatography of the osazones.

Acid Hydrolysis.—The mucilage was heated with 0·5N-sulphuric acid at 90° for 8 hr. After neutralisation with barium carbonate and filtration the concentrated hydrolysate was shown by paper chromatography, using solvent (*a*), to contain galactose (mainly), xylose, and uronic acid, and traces of 3 : 6-anhydrogalactose and hydroxymethylfurfuraldehyde. By visual comparison of the intensity of the galactose and xylose spots with that of the spots from various galactose–xylose mixtures the ratio pentose : hexose was estimated as approximately 1 : 10.

Another portion of the polysaccharide was heated with N-sulphuric acid at 90° for 13 hr. After neutralisation with silver carbonate and filtration, excess of silver was precipitated by hydrogen sulphide. The acid filtrate, after concentration, was shown by paper chromatography, using solvent (*b*), to contain glucurone.

Treatment of D-glucurone with 0·5N-sulphuric acid at 90° for 8 hr. was shown on a paper chromatogram, using solvent (*a*), to cause virtually no decarboxylation to xylose.

A sample of the acid (0·5N) hydrolysate was freed quantitatively from sulphuric acid by means of barium chloride, and sufficient sodium hydroxide was added to make a 10% solution which was refluxed for 90 min. A white precipitate of barium sulphate was formed.

Another portion of the same hydrolysate, after neutralisation with barium carbonate, was treated with sufficient glacial acetic acid to make a 30% solution. To this was added phenylhydrazine and the resulting mixture was heated at 95° for 20 min. After cooling, dilution with water gave a precipitate which was shown on a circular paper chromatogram, using solvent (*c*), to contain galactosazone (mainly) together with xylosazone and 3 : 6-anhydrogalactosazone in approximately equal amounts. Xylosazone was further identified in the mixture of osazones by its characteristic, microscopic, crystalline appearance.

[8] Dickson, Otterson, and Link, *J. Amer. Chem. Soc.*, 1930, **52**, 775.
[9] Albon and Gross, *Analyst*, 1950, **75**, 454.
[10] Irwin and Leaver, *Nature*, 1956, **177**, 1126.
[11] Partridge, *ibid.*, 1949, **164**, 443.
[12] Hough, Jones, and Wadman, *J.*, 1950, 1702.

Action of 0·5N-*Sulphuric Acid on* 3 : 6-*Anhydro*-D-*galactose*.—An authentic sample [13] of the anhydro-sugar was heated with 0·5N-sulphuric acid at 90° for 8 hr. Examination of the product, after neutralisation with barium carbonate and filtration, on a paper chromatogram, using solvent (*a*), indicated a partial conversion into hydroxymethylfurfuraldehyde.

Isolation of 3 : 6-*Anhydro*-D-*galactosazone*.—The mucilage (2·7 g.; dry, ash-free wt.) was heated with 0·5N-sulphuric acid (140 c.c.) at 90° for 8 hr. The hydrolysate, after neutralisation with barium carbonate and filtration, was concentrated to 50 c.c. and treated with phenylhydrazine (15 c.c.), glacial acetic acid (19 c.c.), and ethanol (100 c.c.). The resulting solution was refluxed for 2 hr., the ethanol removed under reduced pressure, and the solution diluted with water to give a precipitate (1·26 g.) which was dissolved in methanol (20 c.c.) and adsorbed on alumina (40 g.). Fractions 1—10 (1·04 g.), eluted by methanol (520 c.c.), yielded, after concentration, material, m. p. 185—189°, which was shown by a circular paper chromatogram, using solvent (*c*), to be substantially galactosazone. The mother-liquors from this were evaporated to dryness giving a residue (0·62 g.) which was dissolved in ether containing a small amount of methanol and re-adsorbed on alumina (20 g.). Fractions 1—2 (28 mg.), eluted by ether (100 c.c.), gave an oil. Fraction 3 (66 mg.), eluted by 9 : 1 ether–methanol (50 c.c.), consisted of 3 : 6-anhydro-D-galactosazone which crystallised from methanol as yellow needles m. p. 200—201°, undepressed on admixture with authentic material.[14] Light absorption: Max. (in 95% aqueous ethanol), 257, 311, 395 mμ ($E^{1\%}_{1\,cm.}$ 558, 294, 592 respectively). The molecular weight (determined from the value of $E^{1\%}_{1\,cm.}$ at 395 mμ, cf. Part V) was 344 (Calc. for $C_{18}H_{20}O_3N_4$: *M*, 340).

Hydrolysis of Barium Galactose 6-*Sulphate and Barium Glucose* 3-*Sulphate*.—The two sulphuric esters [15,16] were, separately, heated at 90° with 0·5N-sulphuric acid. At intervals, portions of the hydrolysates were neutralised with barium carbonate, filtered, concentrated, and examined on a paper chromatogram using solvent (*a*). It was thus shown that after 90 min. barium glucose 3-sulphate had been completely hydrolysed to glucose whereas, after 8 hr., some barium galactose 6-sulphate remained unhydrolysed.

Action of Phenylhydrazine in Acetic Acid Solution on Barium Galactose 6-*Sulphate*.—The galactose sulphuric ester [15] (3·7 g.) was refluxed for 2¼ hr. with phenylhydrazine (14 c.c.), glacial acetic acid (17 c.c.), water (75 c.c.), and ethanol (150 c.c.). Removal of ethanol at reduced pressure followed by dilution with water gave a precipitate (1·5 g.) which was isolated in the centrifuge. Examination of this on a circular paper chromatogram, using solvent (*c*), showed it to contain galactosazone and 3 : 6-anhydrogalactosazone in addition to a large amount of material which did not move from the starting line. The methanol-soluble portion (0·9 g.) of the precipitate was dissolved in methanol (5 c.c.) and adsorbed on alumina (30 g.). Fractions 1—2 (170 mg.), eluted by methanol (40 c.c.), were dissolved in ether containing a small amount of methanol and re-adsorbed on alumina (10 g.). Fraction 1 (90 mg.), eluted by ether (40 c.c.), was an oil. Fraction 2 (62 mg.), eluted by 4 : 1 ether–methanol (25 c.c.), consisted of 3 : 6-anhydro-D-galactosazone, m. p. 200—202°.

First Periodate Oxidation.—Acid hydrolysis of oxidised polysaccharide. The oxidation product, B, obtained by the method of Barry and Dillon [1] from the mucilage, A, was a white powder (Found: ash, 40·2%). It was heated with 0·5N-sulphuric acid at 90° for 1¾ hr. The hydrolysate, after neutralisation with barium carbonate, filtration, and concentration, was shown on a paper chromatogram, using solvent (*a*), to contain galactose, xylose, and uronic acid.

A sample of the acid (0·5N) hydrolysate, after neutralisation with barium carbonate and filtration, was treated with phenylhydrazine and sufficient glacial acetic acid to make a 30% solution and warmed at 95° for 20 min. After cooling, dilution with water gave a precipitate which was shown on a circular paper chromatogram, using solvent (*c*), to contain galactosazone, xylosazone, and glyoxal bisphenylhydrazone together with erythrosazone and/or 3 : 6-anhydrogalactosazone. (The last two osazones have the same R_F values in this solvent system.)

Isoniazid derivative. The oxidised polysaccharide, B (0·14 g.; dry, ash-free wt.), was treated in water (5 c.c.) with a solution of *iso*nicotinhydrazide (isoniazid) (0·5 g.) in water (3 c.c.). After neutralisation with saturated sodium hydrogen carbonate solution, the addition of a large volume of ethanol precipitated a polymeric *substance* which coagulated on being

[13] Haworth, Jackson, and Smith, *J.*, 1940, 620.
[14] Percival, *J.*, 1945, 783.
[15] Percival and Soutar, *J.*, 1940, 1475.
[16] Percival, *J.*, 1945, 119.

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shaken. The product (0·27 g.) was filtered off and washed successively with ethanol and ether (Found : ash, 38·2; N, in ash-free material, 6·1%).

First Degradation.—Isolation of small fragments. The oxidised polysaccharide, B (6 g.; dry, ash-free wt.), was refluxed for 4 hr. with phenylhydrazine (30 c.c.), glacial acetic acid (36 c.c.), water (120 c.c.), and ethanol (240 c.c.). Removal of ethanol at reduced pressure followed by dilution with water gave a precipitate which was removed by filtration. Addition of water to the filtrate yielded an oil which was extracted with difficulty with ether. The extract was washed with dilute acetic acid and water and yielded an oil which was combined with the solid product. Examination on a circular paper chromatogram, using solvent (*c*), showed the combined material to contain galactosazone, xylosazone, and glyoxal bisphenylhydrazone together with erythrosazone and/or 3 : 6-anhydrogalactosazone. The material (6·1 g.) was dissolved in benzene (50 c.c.) and adsorbed on alumina (180 g.). Fractions 4—11 [1·15 g., eluted by benzene (200 c.c.); 0·85 g., eluted by 1 : 1 benzene–ether [200 c.c.)] consisted of glyoxal bisphenylhydrazone, m. p. 159—161°, undepressed on admixture with authentic material. Fraction 27 (0·47 g.), eluted by 1 : 1 ether–ethanol (50 c.c.), was *N*-acetylphenylhydrazine. Fractions 34—38 (0·11 g.), eluted by 9 : 1 ethanol–water (250 c.c.), consisted of erythrosazone which crystallised from benzene as yellow needles, m. p. 153—155°, undepressed on admixture with material obtained from the degradation of oxidised starch (cf. Part IV [7]). Fractions 45—47 (0·23 g.), eluted by 6 : 4 ethanol–water (150 c.c.), were shown by a circular paper chromatogram, using solvent (*c*), to consist mainly of xylosazone. This material did not crystallise well.

Once-degraded polysaccharide, A′. The oxidised mucilage, B (4·6 g.; dry, ash-free wt.), was degraded with phenylhydrazine in acetic acid solution, the same proportions being used as above. A large volume of ethanol precipitated a pale-yellow material, A′ (3·4 g.) (Found : ash, 47·4; S, in ash-free material, 5·9%). This was heated for 8 hr. at 90° with 0·5N-sulphuric acid, and the resulting hydrolysate, after neutralisation with barium carbonate, filtration, and concentration, was shown by paper chromatography, using solvent (*a*), to contain galactose and a trace of xylose. The neutral hydrolysate was treated with phenylhydrazine and sufficient glacial acetic acid to make a 30% solution and the mixture was heated at 95° for 20 min. After cooling, dilution with water gave a precipitate shown on a circular paper chromatogram, using solvent (*c*), to contain galactosazone and 3 : 6-anhydrogalactosazone. Another sample of the once degraded material, A′, was heated with N-sulphuric acid at 90° for 13 hr. After neutralisation with silver carbonate and filtration, excess of silver was removed by hydrogen sulphide. The acid filtrate, after concentration, was examined on a paper chromatogram, with solvent (*b*). No evidence was found of the presence of glucurone.

Second Oxidation and Degradation.—The once degraded material, A′ (1·8 g.; dry, ash-free wt.), was kept with a solution of sodium metaperiodate (5·0 g.) in water (20 c.c.) for 36 hr. The solution was cooled in ice–salt, and the periodate and iodate were reduced by a slow stream of sulphur dioxide. Extraneous material was removed by centrifugation, and addition of ethanol precipitated a pale, buff-coloured material, B′ (4·3 g.) (Found : ash, 59·3%). This was refluxed for 3 hr. with phenylhydrazine (6 c.c.), glacial acetic acid (7 c.c.), water (24 c.c.), and ethanol (48 c.c.). Ethanol was removed from a portion of the mixture and dilution with water produced an opalescence in the solution which deposited, overnight, a small amount of glyoxal bisphenylhydrazone. The main bulk of the mixture was then treated with ethanol to precipitate a yellow material, A″ (1·9 g.) (Found : ash, 50·2; S, in ash-free material, 3·8%). Hydrolysis of this material with 0·5N-sulphuric acid at 90° for 8 hr., followed by neutralisation with barium carbonate and concentration, was shown by paper chromatography, using solvent (*a*), to yield galactose. The neutral hydrolysate was treated with phenylhydrazine and sufficient glacial acetic acid to make a 30% solution which was then heated at 95° for 20 min. After cooling, dilution with water gave a precipitate which was shown on a circular paper chromatogram, using solvent (*c*), to contain galactosazone and 3 : 6-anhydrogalactosazone.

Third Oxidation and Degradation.—The twice degraded material, A″ (0·57 g.; dry, ash-free wt.), was kept for 43 hr. with sodium metaperiodate (1·66 g.) in water (6 c.c.). The product, B″ (96 mg.) (Found : ash, 57·7%), isolated in the same manner as the twice oxidised material, B′, was degraded by being refluxed for 3¾ hr. with phenylhydrazine (2 c.c.), glacial acetic acid (2·3 c.c.), water (8 c.c.), and ethanol (16 c.c.). This mixture was treated with a large volume of ethanol and ether to precipitate a yellow material, A‴ (0·54 g.) (Found : ash, 75·1; S, in ash-free material, 2·4%). Hydrolysis of this material with 0·5N-sulphuric acid at 90° for 8 hr.

and treatment of the neutralised (barium carbonate) hydrolysate with phenylhydrazine and acetic acid for osazone formation gave a product, shown by a circular paper chromatogram, using solvent (*c*), to contain galactosazone and 3 : 6-anhydrogalactosazone.

One of us (J. E. McC.) is a Lasdon Foundation Research Fellow of University College, Dublin.

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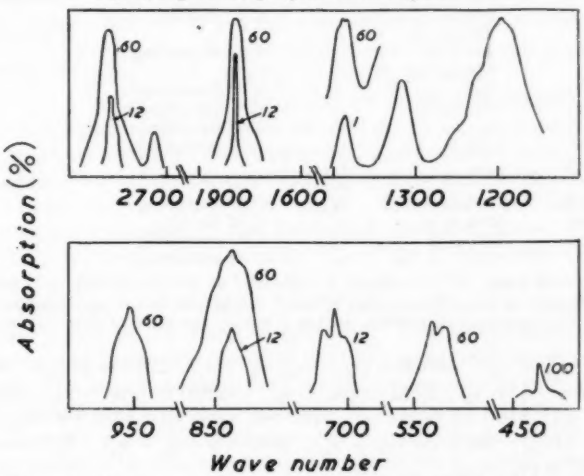
536. *The Infrared and Raman Spectra of Trifluoroacetaldehyde.*

By R. E. DODD, H. L. ROBERTS, and L. A. WOODWARD.

The infrared absorption spectrum of gaseous trifluoroacetaldehyde is measured in the range from 400 to 5000 cm.$^{-1}$. The Raman spectrum of the liquid at $-40°$ is photographed and the states of polarization of the lines determined qualitatively. A probable assignment of the fundamental frequencies is suggested. The torsional frequency appears in the Raman spectrum at 184 cm.$^{-1}$: this corresponds to a potential barrier to internal rotation of 9·8 kcal./mole.

THE infrared spectrum of trifluoroacetaldehyde has been studied by Husted and Albrecht.[1] Since their results are restricted to the rock-salt region it seemed worth while, when a sample of the material was prepared and purified for another purpose,[2] to repeat and

Infrared spectrum of trifluoroacetaldehyde.



The figures beside the curves indicate pressures (mm. Hg) in a 10 cm. cell.

extend the infrared measurements and also to study the Raman spectrum. Of particular interest in the latter was the observation of the torsional frequency.

The only possible symmetry element of the CF_3·CHO molecule is a plane containing the C·CHO grouping and one fluorine atom. The selection rules for this symmetry (point group C_S) allow all 15 fundamental modes in both the infrared and Raman spectra. There are 10 modes of class A' which will give polarized Raman lines; five of these are composed mainly of symmetrical stretching and bending, and will be strongly polarized. The five modes of class A'', which include the torsional vibration, will be depolarized.

[1] Husted and Albrecht, *J. Amer. Chem. Soc.*, 1952, **74**, 5422.
[2] Dodd and Smith, *J.*, 1957, 1465.

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The major bands in the observed infrared spectrum are illustrated in the Figure. The observed Raman frequencies and the infrared frequencies assigned to fundamentals are given in the Table, which also includes data on intensities and the states of polarization of all but the weakest Raman lines. In the rock-salt region the infrared spectrum closely resembles that reported by Husted and Albrecht:[1] asterisks in the Table indicate the frequencies which were also observed by them. The new infrared bands at 1136 and 1212 cm.$^{-1}$ can only be discerned at favourable pressures, since they tend to be obscured by the very strong band at 1197 cm.$^{-1}$. For two of the infrared bands included in the Table no corresponding Raman lines were observed. Both these bands are stronger than those assigned to overtones and combinations: furthermore their frequencies occur in combinations.

Of the infrared bands not assigned to fundamentals, all but two very weak ones are satisfactorily accounted for as overtones or combinations. The observed frequencies (in cm.$^{-1}$) and assignments are as follow: 589 w ($\nu_{10} + \nu_{14}$, $\nu_2 - \nu_{12}$); 860 vw ($2\nu_9$); ~873 vw ($\nu_{15} - \nu_{10}$, $\nu_{12} - \nu_{14}$, $\nu_4 - \nu_9$); ~890 w ($\nu_{15} + \nu_8$, $\nu_{11} - \nu_{14}$); 1012 w ($\nu_{12} - \nu_{15}$, $\nu_{15} + \nu_7$, $\nu_{14} + \nu_8$); 1089 w ($\nu_1 - \nu_2$); ~1436 vw (?); ~1483 vw ($\nu_{10} + \nu_{11}$, $\nu_{13} + \nu_6$); 1544 w ($\nu_{14} + \nu_{11}$, $\nu_8 + \nu_7$); 1681 w ($2\nu_7$); 1735 m ($\nu_{13} + \nu_{12}$, $\nu_9 + \nu_4$); ~1826 m ($\nu_9 + \nu_3$, $\nu_8 + \nu_{15}$, $\nu_{13} + \nu_4$); 1891 w ($\nu_8 + \nu_{12}$); 2036 w ($\nu_7 + \nu_{12}$); 2132 w ($\nu_7 + \nu_4$); 2283 vw ($2\nu_5$); 2305 vw ($\nu_{11} + \nu_2$); ~2350 w ($\nu_5 + \nu_{11}$, $\nu_6 + \nu_3$); 2372 m ($2\nu_{12}$); 2603 w ($\nu_{11} + \nu_4$, $\nu_1 - \nu_{10}$); 2692 w ($\nu_4 + \nu_3$); 2742 m ($\nu_6 + \nu_2$); ~2820 m ($2\nu_7 + \nu_5$); 2907 m ($\nu_5 + \nu_2$); 2986 vw ($\nu_{12} + \nu_2$); 3100 vw ($\nu_4 + \nu_2$); 3165 vw ($\nu_3 + \nu_2$); 3488 vw ($2\nu_5 + \nu_{12}$); 3565 m ($2\nu_2$); 3606 vw ($3\nu_{12}$); 3693 vw ($\nu_7 + \nu_1$); 4065 vw ($\nu_{12} + \nu_1$); 4216 vw (?); 4509 vw ($2\nu_2 + \nu_6$); 4647 w ($\nu_2 + \nu_1$).

Fundamental frequencies of trifluoroacetaldyde.

Observed frequencies (cm.$^{-1}$)		Assignment		
Infrared	Raman		Class *A'* (in-plane)	Class *A''* (out-of-plane)
	184 w	ν_{15}		Torsion
	266 w	ν_{10}	CF_3 rocking	
	320 m, dp	ν_{14}		CF_3 rocking
430 (2)	432 s, p	ν_9	C–C=O bending	
533 (11)	528 m, dp	ν_{13}		CF_3 deformation
706* (72)	708 s, p	ν_8	CF_3 deformation	
839* (43)	837 vs, p	ν_7	CF_3 deformation	
957* (11)		ν_6	C–C stretching	
1136 (15)	1145 w	ν_5	C–F stretching	
1197* (915)	1200 w	ν_{12}		C–F stretching
1212 (80)		ν_{11}		C–H bending
1309* (203)	1305 vw	ν_4	C–F stretching	
1385* (79)	1383 w, p	ν_3	C–H bending	
1784* (81)	1770 s, p	ν_2	C=O stretching	
2870* (40)	2901 s, p	ν_1	C–H stretching	

vw = very weak, w = weak, m = medium, s = strong, vs = very strong, p = polarized, dp = depolarized. Figures in parentheses after infrared fundamentals are approximate molar extinction coefficients. For Raman lines marked neither p nor dp the state of polarization is uncertain.

The Table gives the suggested assignment which can be made by comparison with the spectra of $CF_3{\cdot}CHCl_2$;[3] $CF_3{\cdot}CF_2Cl$, $CF_3{\cdot}CFCl_2$;[4] $CF_3{\cdot}CHF_2$;[5] $CF_3{\cdot}CN$;[6] CF_3Br, CF_3I;[7] $CCl_3{\cdot}CHO$, $CBr_3{\cdot}CHO$;[8] $CH_3{\cdot}CHO$.[9] It is emphasized that the descriptions of the modes given in the last two columns of the Table are only approximate. In some of the modes considerable mixing must occur.

[3] Nielsen, Liang, and Smith, *J. Chem. Phys.*, 1953, **21**, 1060.
[4] Nielsen, Liang, Smith, and Smith, *ibid.*, p. 383.
[5] Nielsen, Claassen, and Moran, *ibid.*, 1955, **23**, 329.
[6] Edgell and Potter, *ibid.*, 1956, **24**, 80.
[7] Edgell and May, *ibid.*, 1954, **22**, 1808.
[8] Seewann-Albert, *Acta Phys. Austriaca*, 1947—8, **1**, 346.
[9] Pitzer and Weltner, *J. Amer. Chem. Soc.*, 1949, **71**, 2842.

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The frequency 2870 cm.$^{-1}$ (infrared), 2901 (Raman) can at once be assigned to C–H stretching and is close to the values 2863 and 2848 cm.$^{-1}$ for CCl_3·CHO and CBr_3·CHO respectively. The carbonyl stretching frequency occurs at 1784 cm.$^{-1}$ (infrared), 1770 (Raman). The value rises with increasing electronegativity of the attached groups, thus: 1740 (CH_3·CHO), 1742 (CBr_3·CHO), 1762 (CCl_3·CHO). This frequency is even higher in the acid halides, the value being 1866 in acetyl fluoride [10] and about 1890 in fully fluorinated acid fluorides.[11] The C=CH_2 stretching frequency is similarly affected: it occurs at 1649 cm.$^{-1}$ in propene [12] and at 1670 in CF_3·CH=CH_2.[13]

The next group of five fundamentals comprises three C–F stretching modes ($2A' + A''$) and two C–H bending modes ($A' + A''$). In CCl_3·CHO and CBr_3·CHO, where there are no close neighbours, the two C–H bending frequencies occur at 1350 and 1025 cm.$^{-1}$ and at 1352 and 1000 cm.$^{-1}$. In CF_3·$CHCl_2$ the values 1325 and 1192 are assigned to these modes. On the other hand the very great intensity of the 1197 cm.$^{-1}$ band of CF_3·CHO in the infrared spectrum and the very low intensity in the Raman spectrum indicate that it is a C–F stretching mode; and the same probably applies to the infrared band at 1309 cm.$^{-1}$. The C–H bending modes are accordingly assigned to 1385 and 1212 cm.$^{-1}$, the remaining C–F stretching frequency being at 1136 cm.$^{-1}$. Interchange of ν_5 and ν_{11} is, however, equally reasonable.

The assignment of 957 cm.$^{-1}$ to the C–C stretching mode is consistent with similar assignments in CH_3·CHO (1114 cm.$^{-1}$, strong in infrared; very weak in Raman), CCl_3·CHO (985 cm.$^{-1}$, weak in Raman), and CBr_3·CHO (979 cm.$^{-1}$, weak in Raman). The next four frequencies comprise the C–C=O bending mode (A') and three CF_3 deformation modes ($2A' + A''$). The C–C=O bending frequency is given as 525 cm.$^{-1}$ in CH_3·CHO and 618 cm.$^{-1}$ in CCl_3·CHO. The CF_3 deformation frequencies of the other molecules mentioned all lie in the region 840—550 cm.$^{-1}$, and our assignment is consistent with this. Owing to the closeness of their frequencies, none of these modes will be even approximately pure. The frequencies 320 and 266 cm.$^{-1}$ are assigned to CF_3 rocking.

The envelopes of seven of the infrared bands are fairly well defined. As can be seen from the Figure, the bands at 430, 706, 839, and 957 cm.$^{-1}$, and probably those at 1385 and 2870 cm.$^{-1}$, have *PQR* contours. The apparent *PR* separation varies somewhat but is clearly seen as about 16 cm.$^{-1}$ at 430 and 706 cm.$^{-1}$. The band at 533 cm.$^{-1}$ shows no zero branch and a smaller *PR* separation of 12 cm.$^{-1}$. These facts are not easily reconciled with the assignments suggested in the Table and discussed above. Assuming point-group C_s with the bond lengths C–F = 1·36, C–C = 1·54, C–H = 1·09, C=O = 1·21 Å and the bond angles C–C–F = C–C–H = 109° 28′, C–C=O = 119°, we calculate the principal moments of inertia to be $I_x = 101$, $I_y = 172$, and $I_z = 174$ a.m.u. (atomic mass units) Å^2 (x- and y-axes in the plane of symmetry, z-axis perpendicular thereto). No decision can be made as to the orientation of the CHO group with respect to the CF_3, since the moments of inertia are identical for both configurations of point group C_s so long as the CF_3 group retains its 3-fold symmetry about the C–C axis. Increase of the C–C=O angle to 130° gives $I_x = 101$, $I_y = 177$, and $I_z = 179$ a.m.u. Å^2. According to these results, which show the models to be near-symmetric tops, the class A' modes are expected to have mixed type A and type B contours, and the class A'' modes type C. In view of the fairly pronounced Q branches to be expected for both type A and type C, the observation of *PQR* contours provides no criterion for assignment. It may be significant, however, that the bands for which *PQR* contours are observed are all (with the exception of that at 957 cm.$^{-1}$) assigned to class A' on the evidence of the polarization of the corresponding Raman lines; whereas the band at 533 cm.$^{-1}$ has the appearance and about the expected *PR* separation of type B, at variance with its assignment to class A'' if the axis of intermediate moment of inertia is in the symmetry plane. Thus the contours would accord

[10] Dodd, unpublished observation.
[11] Haszeldine, *Nature*, 1951, **168**, 1028.
[12] Kilpatrick and Pitzer, *J. Res. Nat. Bur. Stand.*, 1947, **38**, 191.
[13] Haszeldine, personal communication.

more satisfactorily with the suggested assignments if the dimensions of the molecule were such that I_z were the intermediate moment. We have not investigated what variations (if any) of the model would lead to this result.

The frequency 184 cm.$^{-1}$ remains and is assigned to the torsional mode, *i.e.*, twisting about the C–C bond. This is of particular interest since it allows an estimate of the height of the potential barrier preventing free rotation. If it is assumed that the potential energy for this type of motion is given by $\frac{1}{2}V_0(1 - \cos 3\theta)$, where V_0 is the potential barrier separating each of the three minima of potential energy and θ is the torsional angle, and if it is further assumed that the vibration is simple harmonic, then it follows [14] that $\nu_{15} = 3(V_0B_1B_2/B)^{\frac{1}{2}}$, where B_1, B_2, and B are respectively the rotational constants for the two groups CF_3 and CHO and for the whole molecule about the torsion axis. Reasonable values for the molecular dimensions give moments of inertia about the torsion axis of 165×10^{-40} g. cm.^{2} for CF_3 and $30{\cdot}2 \times 10^{-40}$ g. cm.^{2} for CHO. These lead to the value 9·8 kcal./mole for the height of the potential barrier, which may be compared with 10·1 kcal./mole for $CF_3{\cdot}CHCl_2$, 9·1 for $CF_3{\cdot}CF_2Cl$, and 11·9 for $CF_3{\cdot}CCl_3$.[15] Pitzer and Weltner [9] give a value near 1 kcal./mole for $CH_3{\cdot}CHO$, and more recently Wilson [16] has estimated it as 1·13 : for ethane the figure [17] is about 2·9 kcal./mole. The high values for the fluorinated compounds may arise from the large electronegativity of the fluorine and the consequent strong repulsions between non-bonded atoms. The effect is more marked in torsion against a CHO group than against a CH_3. Thus partial fluorination of ethane leads to only small increases in the potential barrier, the values for $CHF_2{\cdot}CH_3$ and $CH_2F{\cdot}CH_3$ being respectively 3·18 and 3·31 kcal./mole.[16] Unfortunately no independent thermodynamic data are available for trifluoroacetaldehyde to permit the spectroscopic conclusions to be checked.

Experimental

Trifluoroacetaldehyde was prepared by Rosenmund reduction of the acid chloride as recommended by Brown and Musgrave : [18] further details are given elsewhere.[3] The infrared absorption spectrum of the vapour was measured in the region 400—5000 cm.$^{-1}$ with a Grubb-Parsons double-beam spectrometer, prisms of potassium bromide, sodium chloride, and lithium fluoride being used. The Raman spectra were photographed with the apparatus previously described [19] (Toronto arc excitation, Hilger E 518 spectrograph). The states of polarization of all but the weakest lines were determined qualitatively by the method of incident polarized light, by use of suitable Polaroid cylinders surrounding the Raman vessel. The sample (*ca.* 0·5 ml.) was distilled *in vacuo* into the Raman vessel and maintained liquid at −40°. The exciting line was Hg 4358 Å : a sodium nitrite filter was used to reduce the intensity of primary lines of shorter wavelength. Exposures up to 8 hr. were given, and Kodak Special Scientific plates used. The recorded frequencies, determined in the usual manner with a copper arc spectrum as standard, are probably correct to within ±3 cm.$^{-1}$ for strong, sharp lines. For the weaker lines the errors may be larger.

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[14] Herzberg, "Infra-red and Raman Spectra," Van Nostrand, New York, 1945, p. 226.
[15] Luft, *J. Chem. Phys.*, 1954, **22**, 155.
[16] Wilson, *Spectroscopia Molecular*, 1956, **5**, 44.
[17] Pitzer, *Discuss. Faraday Soc.*, 1951, **10**, 66.
[18] Brown and Musgrave, *J.*, 1952, 5049.
[19] Rolfe and Woodward, *Trans. Faraday Soc.*, 1954, **50**, 1030.

537. ^{14}C-*Labelled Polycyclic Aromatic Hydrocarbons. Part I. The Synthesis of* [9-^{14}C]*Anthracene and Some Methyl-substituted Anthracenes.*

By J. R. Catch and E. A. Evans.

[9-^{14}C]Anthracene and three of its monomethyl derivatives have been synthesised by a new method involving only three radiochemical steps from $^{14}CO_2$.

This series of papers describes syntheses of polycyclic aromatic hydrocarbons, particularly some having carcinogenic activity,[1] labelled in a ring with ^{14}C, by methods which involve few radioactive stages and give good yields on a small scale, thus affording high specific activities.

[9-^{14}C]Anthracene [2] was prepared by Stevens and Holland [3] from *o*-tolu[^{14}C]ic acid by a six-stage synthesis, in an overall radiochemical yield of 58·5%. We describe a synthesis having only three radioactive stages, starting with the Grignard reagent from *o*-benzylbromobenzene which gave *o*-benzylbenz[^{14}C]oic acid in 95% yield on carboxylation with $^{14}CO_2$. Ring closure of the acid with anhydrous hydrogen fluoride gave 90—99% of anthrone which on reduction with zinc dust in sodium hydroxide gave [9-^{14}C]anthracene in 73·5% yield (69% based on carbon dioxide). The overall radiochemical yield from $^{14}CO_2$ was 72·5%. Anthrone with methylmagnesium iodide in ether–benzene gave 9-methyl[9-^{14}C]anthracene in 69% overall radiochemical yield.

1-Methyl[10-^{14}C]anthracene and 2-methyl[9-^{14}C]anthracene were prepared similarly from the appropriate bromo-compound, in 67% and 52% overall radiochemical yield respectively from $^{14}CO_2$.

The bromo-compounds (I) were prepared by treating *o*-bromobenzaldehyde with the appropriate arylmagnesium bromide and reducing the resulting secondary alcohol with red phosphorus and iodine in glacial acetic acid.

o-Bromo-3-methylbenzylbenzene gave, on carboxylation with $^{14}CO_2$, a 93% yield of the acid, but cyclisation of this with anhydrous hydrogen fluoride followed by reduction of the product gave 2-methyl[10-^{14}C]anthracene (chemically identical with 3-methylanthracene) in a yield of only 25%. No 1-methylanthracene was isolated, indicating the efficiency of the steric hindrance.

Small yields of anthracene, probably generally labelled with ^{14}C, have been obtained by neutron bombardment of acridine,[4] together with larger amounts of labelled acridine. The yields and specific activities are, however, much too low to make this reaction a useful source of tracer compounds, and this is true of many comparable radiation syntheses of ^{14}C-compounds.[5]

Experimental

M. p.s were observed on a Kofler block and are corrected. Microanalyses were carried out by Drs. G. Weiler and F. B. Strauss, Oxford, and Mr. D. A. Lambie, Radiochemical Centre. Grignard reagents were prepared in an atmosphere of dry oxygen-free nitrogen. Radioactive samples were measured as layers of barium [^{14}C]carbonate of infinite thickness, formed by burning samples in a stream of oxygen and absorbing the $^{14}CO_2$ in saturated aqueous barium hydroxide.

o-Benzylbromobenzene.—*o*-Bromobenzaldehyde (9 g.) in anhydrous ether (25 ml.) was added

[1] Catch and Evans, *Chem. and Ind.*, 1957, 78; cf. Bhargava, Hadler, and Heidelberger, *J. Amer. Chem. Soc.*, 1955, **77**, 2877; Wiest and Heidelberger, *Cancer Res.*, 1953, **13**, 250.
[2] For previous syntheses of anthracene see "Elsevier's Encyclopædia of Organic Chemistry," Ed. Josephy and Radt, New York, 1946, Vol. XIII, p. 199.
[3] Stevens and Holland, *Science*, 1950, **112**, 718.
[4] Wolf and Anderson, *J. Amer. Chem. Soc.*, 1955, **77**, 1608.
[5] Cf. Schrodt and Libby, *ibid.*, 1956, **78**, 1267.

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to phenylmagnesium bromide (from magnesium, 1·3 g., and bromobenzene, 8 g.) in ether (30 ml.). The solution was stirred at room temperature for 30 min. and then treated with excess of saturated ammonium chloride. The ether layer was separated and the aqueous layer extracted with ether (2 × 20 ml.), the ether layers were combined, and most of the solvent was removed. The residual liquid was dissolved in glacial acetic acid (150 ml.), iodine (3 g.), red phosphorus (3 g.), and water (15 ml.) were added, and the mixture was refluxed for 24 hr. When cold, the solution was filtered and ice added to the filtrate. Most of the acetic acid was neutralised with 10% aqueous sodium hydroxide and the solution extracted with ether (3 × 100 ml.). The ether extracts were washed several times with 10% aqueous sodium hydroxide and with water (2 × 100 ml.), dried (Na_2SO_4–K_2CO_3), and distilled, giving *o*-benzylbromobenzene (7·5 g., 62%), b. p. 82°/10^{-3} mm., n_D^{25} 1·6060 (Bergmann [6] gives b. p. 175°/22 mm.) (Found: C, 63·1; H, 4·7; Br, 31·9. Calc. for $C_{13}H_{11}Br$: C, 63·2; H, 4·45; Br, 31·3%).

o-*Benzylbenzoic Acid*.—$^{14}CO_2$ generated from barium [^{14}C]carbonate (0·564 g., 1 mc) with concentrated sulphuric acid in a closed vacuum system was condensed into a Grignard solution prepared from *o*-benzylbromobenzene (0·8 g.) and magnesium (85 mg.) in ether (15 ml.). The solution was first frozen in liquid nitrogen, then held in a vacuum for 15 min., the $^{14}CO_2$ condensed in, and the solution stirred at room temperature for 30 min., refrozen, and stirred for a further 15 min. at room temperature. Water (15 ml.) and concentrated hydrochloric acid (until acid) were added, the ether layer separated, and the aqueous layer extracted with ether (3 × 20 ml.). The combined ether layers were extracted with 2N-sodium hydroxide (4 × 25 ml.), and the alkaline extracts acidified with concentrated hydrochloric acid. After slow cooling to 0° the crude labelled *o*-benzylbenzoic acid was filtered off (m. p. 108—111°); it crystallised in needles (0·57 g., 95%) (*a*) from aqueous ethanol (m. p. 114°), which were pure enough for the next stage. A sample crystallised to constant m. p. had m. p. 115—116° (lit.,[7] m. p. 117°). To the mother-liquors was added inactive carrier *o*-benzylbenzoic acid (200 mg.) and on concentration and crystallisation more acid (270 mg.), m. p. 108—110° (*b*), was obtained.

[9-^{14}C]*Anthrone*.—*o*-Benzylbenzoic acid (570 mg., *a* above) was treated in a platinum crucible with anhydrous fluoride (*ca.* 8—10 ml.), left at room temperature for 10 min. with occasional stirring, and then poured on ice. The anthrone (470 mg., 90%), m. p. 154—155° (Fieser and Hershberg [8] give m. p. 154—156°), was filtered off. Cyclisation of *o*-benzylbenzoic acid (220 mg., *b*) gave anthrone (200 mg., 99%). In other experiments yields between 90 and 99% were obtained.

[9-^{14}C]*Anthracene*.—Anthrone (150 mg., prepared from acid *a*) was refluxed with zinc dust (1 g.) (activated by copper sulphate), 2N-sodium hydroxide (10 ml.), and toluene (5 ml.) for 3 hr. The toluene layer was separated, the aqueous layer extracted with benzene (3 × 5 ml.), and the excess of zinc dust washed with hot benzene (3 × 5 ml.). The combined extract and washings were dried (Na_2SO_4), and the solvents removed. The residual solid crystallised from toluene, giving [9-^{14}C]anthracene (100 mg., 73·5%), m. p. and mixed m. p. 214—215° (Baxter and Hale [9] give m. p. 216·2—216·4°), 400 μc/mmole. Reduction of anthrone (200 mg.) prepared from acid *b* gave anthracene (75 mg.), m. p. 215°, 48·6 μc/mmole.

9-*Methyl*[9-^{14}C]*anthracene*.—Anthrone (100 mg.) from acid *a* in benzene (5 ml.) was added to methylmagnesium iodide (from magnesium, 72 mg., and methyl iodide, 430 mg.) in ether (10 ml.). The mixture was refluxed for 3—4 hr., then cooled, and excess of hydrochloric acid (50% v/v) was added. The organic layer was separated and the aqueous layer extracted with benzene (2 × 10 ml.). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure. The residual solid crystallised from aqueous ethanol, to give 9-methyl-[9-^{14}C]anthracene (68 mg., 70%), m. p. 77—79°, 414 μc/mmole. After two recrystallisations a sample of m. p. and mixed m. p. 78—79° was obtained (Sieglitz and Marx [10] give m. p. 81·5°).

o-*Bromo-2-methylbenzylbenzene*.—*o*-Bromobenzaldehyde (5 g.) in ether (25 ml.) was added dropwise to *o*-tolymagnesium bromide (from magnesium, 0·72 g., and *o*-bromotoluene, 5 g.) in ether (25 ml.). Isolation of the secondary alcohol and reduction with phosphorus (2 g.) and iodine (2 g.) as above gave o-*bromo-2-methylbenzylbenzene* (5·0 g., 71%), b. p. 105°/10^{-3} mm., n_D^{19} 1·6047 (Found: C, 63·8; H, 5·0; Br, 30·5. $C_{14}H_{13}Br$ requires C, 64·4; H, 5·0; Br, 30·6%).

o-2-*Methylbenzylbenz*[^{14}C]*oic Acid*.—$^{14}CO_2$ (from barium[^{14}C]carbonate, 0·985 g., 150 μc)

[6] Bergmann, *J. Org. Chem.*, 1939, **4**, 1.
[7] Fischer and Schmidt, *Ber.*, 1894, **27**, 2788.
[8] Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1939, **61**, 1272.
[9] Baxter and Hale, *ibid.*, 1937, **59**, 506.
[10] Sieglitz and Marx, *Ber.*, 1923, **56**, 1619.

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was condensed into the Grignard reagent from *o*-bromo-2-methylbenzylbenzene (1·85 g.), magnesium (0·18 g.), and iodine (1 crystal) in a closed vacuum-system. Isolation of the acid as above gave *o*-2-methylbenzylbenz[^{14}C]oic acid (1·2 g., 100%), m. p. 116—119°, which was used for the next stage without further purification. A sample crystallised in plates from aqueous ethanol had m. p. and mixed m. p. 125—126° (Bergmann and Loewenthal [11] give m. p. 128—130°).

1-*Methyl*[10-^{14}C]*anthracene*.—*o*-2-Methylbenzylbenz[^{14}C]oic acid (1·2 g.) was stirred in anhydrous hydrogen fluoride (30 ml.) for 30 min. The cyclised product, isolated as above, was reduced under reflux for 6 hr. with zinc dust (5 g.), 5N-sodium hydroxide (50 ml.), and toluene (25 ml.). Isolation as for anthracene gave 1-methylanthracene (0·62 g.), m. p. 83—84°, which after one crystallisation from methanol (charcoal) gave colourless needles (0·57 g.), 31 μc/mmole, m. p. 84—85° (Fischer and Sapper [12] give m. p. 85—86°).

o-*Bromo*-4-*methylbenzylbenzene*.—This *compound*, prepared in 64% yield from *o*-bromobenzaldehyde (5 g.) and *p*-tolylmagnesium bromide, as above, had b. p. 103—104°/10^{-4} mm., n_D^{20} 1·6002 (Found: C, 64·7; H, 5·3; Br, 29·7%).

o-4-*Methylbenzylbenz*[^{14}C]*oic Acid*.—Prepared quantitatively from $^{14}CO_2$ (5 mmole, 150 μc) and the Grignard reagent from *o*-bromo-4-methylbenzylbenzene, this acid had m. p. 127—129°. A sample recrystallised from aqueous ethanol had m. p. and mixed m. p. 130—131° (Found: C, 80·2; H, 6·6. Calc. for $C_{15}H_{14}O_2$: C, 79·7; H, 6·2%) (Bergmann and Loewenthal [11] give m. p. 133·5—134°).

2-*Methyl*[9-^{14}C]*anthracene*.—Cyclisation of the preceding acid (1·2 g.) and reduction as above gave 2-methyl[9-^{14}C]anthracene (0·6 g.) which was isolated by sublimation *in vacuo* and crystallised from methanol in plates (0·5 g., 52% from $^{14}CO_2$), m. p. and mixed m. p. 204—205° (lit.,[13] 207°), 30 μc/mmole (Found: C, 93·6; H, 6·3. Calc. for $C_{15}H_{12}$: C, 93·7; H, 6·3%). No significant amounts of acid were recovered from the aqueous alkaline layer after the reduction.

o-*Bromo*-3-*methylbenzylbenzene*.—Prepared from *o*-bromobenzaldehyde (4 g.) and *m*-tolylmagnesium bromide, as above, this *compound* (3·8 g., 67%) had b. p. 103—104°/10^{-3} mm., n_D^{20} 1·6016 (Found: C, 65·1; H, 4·9; Br, 29·9%).

o-3-*Methylbenzylbenz*[^{14}C]*oic Acid*.—Prepared from $^{14}CO_2$ (5 mmole, 150 μc) and the appropriate Grignard reagent in 93% yield, the *acid* crystallised from aqueous ethanol in plates, m. p. and mixed m. p. 101—102° (Found: C, 79·5; H, 6·3%).

2-*Methyl*[10-^{14}C]*anthracene*.—Cyclisation of the preceding acid and reduction of the product gave, after chromatography of the hydrocarbons on alumina in benzene and crystallisation from methanol, 2-methyl[10-^{14}C]anthracene (250 mg., 25%), m. p. and mixed m. p. 204—205°, 30 μc/mmole. No other identifiable products were isolated.

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[11] Bergmann and Loewenthal, *Bull. Soc. chim. France*, 1952, **19**, 66.
[12] Fischer and Sapper, *J. prakt. Chem.*, 1911, **83**, 203; Keimatsu, Hirano, and Yoshimi, *J. Pharm. Soc. Japan*, 1930, **50**, 644.
[13] Fischer, *J. prakt. Chem.*, 1909, **79**, 555; Scholl and Lenko, *Monatsh*, 1918, **39**, 237.

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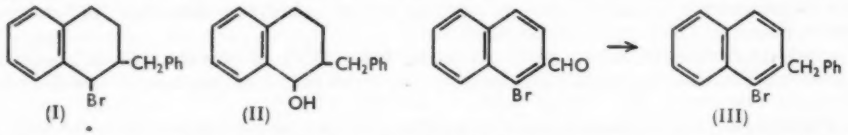
538. ^{14}C-*Labelled Polycyclic Aromatic Hydrocarbons. Part II.*[1] *The Synthesis of* 1 : 2-*Benzanthracene and Some Methyl-substituted* [^{14}C]-*Benzanthracenes.*

By E. A. Evans.

Syntheses from $^{14}CO_2$ of 1 : 2-benzanthracene and 5-methyl- and 9 : 10-dimethyl-1 : 2-benzanthracene labelled with ^{14}C in the 9- or 10-position are described. Alternatively 1 : 2-[^{14}C]benzanthracene may be prepared from 1-naphth[^{14}C]aldehyde.

Previous syntheses of [^{14}C]benzanthracenes have employed Wagner–Meerwein rearrangement of 5-(hydroxy[^{14}C]methyl)-2 : 3-benzofluorene, which has given 1 : 2-benzanthracene labelled in the 5- and 6-positions,[2] in 76% overall yield from $^{14}CO_2$, or neutron irradiation of benzacridine,[3] which gave only poor yields. To prepare the bromo-compound (I) was first tried. 2-Benzylidenetetralone was reduced with lithium aluminium hydride to 2-benzyl-1 : 2 : 3 : 4-tetrahydro-1-naphthol (II), both the carbonyl group and the exo-ethylenic bond being reduced under the conditions employed, as has been observed in other cases.[4] This same hydroxy-compound was obtained by lithium aluminium hydride reduction of 2-benzyltetralone. In an attempt to replace the hydroxyl group in (II) by a bromine atom, with phosphorus tribromide in toluene, there was ready loss of hydrogen bromide and on distillation only 2-benzyl-3 : 4-dihydronaphthalene was obtained, which was identified by its ultraviolet absorption spectrum and dehydrogenation with 5% palladium–charcoal to 2-benzylnaphthalene. It was thus necessary to aromatise the ring system completely in the bromide (I) and so prevent dehydrobromination. 2-Benzyl-1-bromonaphthalene was prepared from phenylmagnesium bromide and 1-bromo-2-naphthaldehyde,



the resulting secondary alcohol being reduced to (III) with iodine and red phosphorus in glacial acetic acid. In a Grignard reaction the bromo-compound (III) gave an 84—86% yield of 2-benzyl-1-naphthoic acid, which was cyclised with anhydrous hydrogen fluoride and on reduction with zinc in sodium hydroxide gave 1 : 2-[9-^{14}C]benzanthracene (83% radiochemical yield, from $^{14}CO_2$).

In an alternative synthesis the aldehyde (IV) was prepared by carboxylation of 1-naphthylmagnesium bromide with $^{14}CO_2$, reduction of the labelled acid with lithium aluminium hydride, and oxidation of the resulting 1-naphthylmethyl alcohol with tetrachloro-1 : 2-benzoquinone [5] to the aldehyde which was isolated as semicarbazone in 62% yield. Oxidation of the alcohol with chromium trioxide in pyridine [6] gave an 86% yield of 1-naphthaldehyde, the overall yield from $^{14}CO_2$ being 65—70%. The labelled 1-naphthaldehyde with *o*-tolylmagnesium bromide gave the alcohol (V), which was pyrolysed directly with zinc dust at 410°, or converted into the ketone (VI) by chromic acid in sulphuric acid [7] and then pyrolysed. In both methods the pyrolysis yielded only 30% of 1 : 2-benzanthracene. The overall radiochemical yield from $^{14}CO_2$ in the five stages was however only 6—8%.

[1] Part I, preceding paper.
[2] Collins, Burr, and Hess, *J. Amer. Chem. Soc.*, 1951, **73**, 5176.
[3] Muxart, *Compt. rend.*, 1956, **242**, 2457.
[4] Hochstein and Brown, *J. Amer. Chem. Soc.*, 1948, **70**, 3484; Phillips and Mentha, *ibid.*, 1956, **78**, 140; cf. following paper.
[5] Cf. Braude, Linstead, and Wooldridge, *J.*, 1956, 3070.
[6] Cf. Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422; Braude, Forbes, and Evans, *J.*, 1953, 2202.
[7] Cf. Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548.

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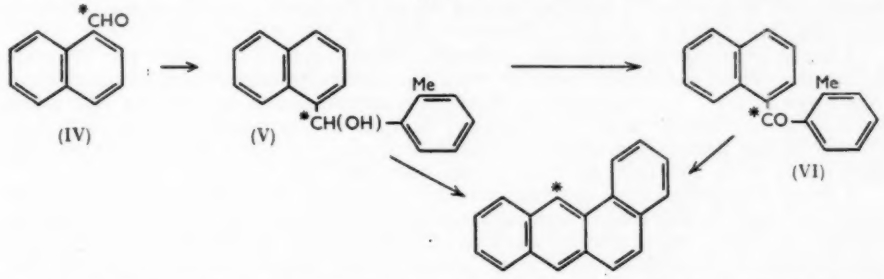
For the synthesis of 1 : 2-[10-^{14}C]benzanthracene, 1-2′-bromobenzylnaphthalene (VII; X = Br) was prepared from *o*-bromobenzaldehyde and 1-naphthylmagnesium bromide, followed by reduction with red phosphorus and iodine. Carboxylation of the Grignard reagent from the bromo-compound (VII) with $^{14}CO_2$ gave the [^{14}C]acid (VIII) in 80% yield. This was cyclised with anhydrous hydrogen fluoride and then reduced to 1 : 2-[10-^{14}C]benzanthracene with zinc in sodium hydroxide. The overall radiochemical yield from $^{14}CO_2$ was 24%, which is considerably lower than that in the corresponding synthesis of 1 : 2-[9-^{14}C]benzanthracene owing to the relatively poor yield in the cyclisation stage, which had previously been extensively investigated by Fieser and Hershberg.[8] An attempt to cyclise the acid (VIII) with boron trifluoride in ether gave only unchanged

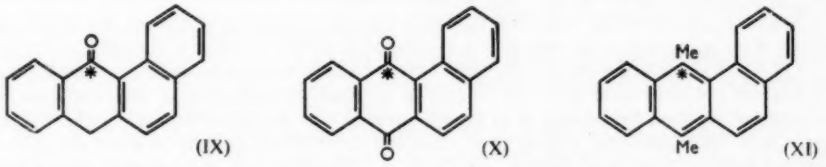


acid. The chloro-compound[9] (VII; X = Cl) did not react with magnesium and could not be cross-metallated with *n*-butyl-lithium, but reacted with lithium and on carboxylation gave <30% of impure acid (VIII).

An attempt to convert 1 : 2-benzanthracene into 9 : 10-dimethyl-1 : 2-benzanthracene (XI) by treating its dilithio-derivative with methyl bromide and dehydrogenating the product[10] failed on the semimicro-scale employed, giving only mixtures.

(VII) α-$C_{10}H_7$·CH_2·C_6H_4X-*o* ⟶ α-$C_{10}H_7$·CH_2·C_6H_4·$^{14}CO_2H$-*o* (VIII)

9 : 10-Dimethyl-1 : 2-[9-^{14}C] benzanthracene was best prepared[11] by oxidising 1 : 2-benzanthracene or the benzanthrone (IX) to 1 : 2-benzanthraquinone (X) and converting this by methylmagnesium iodide followed by hydriodic acid into 10-iodomethyl-9-methyl-1 : 2-benzanthracene, which on treatment with stannous chloride in dioxan gave 9 : 10-dimethyl-1 : 2-[9-^{14}C]benzanthracene. The overall radiochemical yield from the ketone (IX) or benzanthracene was 18%. Reaction of the ketone (IX) with methylmagnesium iodide failed to give 9-methyl-1 : 2-benzanthracene.



5-Methyl-1 : 2-[9-^{14}C]benzanthracene was prepared from 1-bromo-2-2′-methylbenzylnaphthalene, by carboxylation of the Grignard reagent, cyclisation of the resulting acid with anhydrous hydrogen fluoride, and reduction of the keto-group, as in the above cases. The overall radiochemical yield from $^{14}CO_2$ was 59%.

In the syntheses described above, cyclisations of the acids are only likely to take place

[8] Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1937, **59**, 1028.
[9] Bradsher, *ibid.*, 1940, **62**, 1077; Vingiello, Borkovec, and Shulman, *ibid.*, 1955, **77**, 2320.
[10] Mikhailov, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1946, 619.
[11] Cf. Sandin and Fieser, *J. Amer. Chem. Soc.*, 1940, **62**, 3100.

in one position. In no case was any cyclisation to the *peri*-naphthalene position observed. In the formation of most of the Grignard reagents it was necessary to add 1—2 drops of methyl iodide to initiate the reaction. Although the minimum quantity of methyl iodide was used, on a small scale this reduces the yield of required acid owing to the formation of a little acetic acid from the methylmagnesium iodide. This effect could be reduced by making the Grignard reagent on a larger scale and taking an aliquot portion for the carboxylation.

Experimental

For general methods see Part I.

1-*Bromo*-2-*methylnaphthalene*.—2-Methylnaphthalene (75 g.) was brominated in carbon tetrachloride as described by Hall and Mitchell,[12] giving 1-bromo-2-methylnaphthalene (97·5 g.), b. p. 114—116°/10^{-2} mm. (Hall and Mitchell [12] give b. p. 112—117°/1 mm.).

1-*Bromo*-2-*bromomethylnaphthalene*.—1-Bromo-2-methylnaphthalene (50 g.), *N*-bromosuccinimide (40 g.), and benzoyl peroxide (0·5 g.) in carbon tetrachloride (100 g.) were refluxed in nitrogen for 2 hr. The solution was diluted with carbon tetrachloride (50 ml.), then filtered hot and the succinimide washed several times with hot carbon tetrachloride (total 100 ml.). The solvent was allowed to evaporate overnight in air, giving 1-bromo-2-bromomethylnaphthalene (53 g.), m. p. 107—108° (lit.,[13] m. p. 103—105°, 106—108°).

1-*Bromo*-2-*naphthaldehyde*.—1-Bromo-2-bromomethylnaphthalene (40 g.) in boiling glacial acetic acid (100 ml.) was treated with hexamine (20 g.) and heated for about 30 sec., until the solution was clear. Water (75 ml.) was added and the solution allowed to cool. 1-Bromo-2-naphthaldehyde recrystallised from acetic acid as yellow prisms (15·5 g.), m. p. 117—118° (Hewett [14] gives m. p. 117—118°).

1-*Bromo*-2-2′-*methylbenzylnaphthalene*.—1-Bromo-2-naphthaldehyde (5 g.), in benzene (30 ml.) and ether (20 ml.), was added to *o*-tolylmagnesium bromide (from magnesium, 0·6 g., and *o*-bromotoluene, 4 g.) in ether (20 ml.). The solution was heated under reflux for 3 hr., then cooled, and excess of saturated aqueous ammonium chloride added. The organic layer was separated and most of the solvent distilled off under reduced pressure. The residue was dissolved in acetic acid (100 ml.), and iodine (3 g.), red phosphorus (3 g.), and water (20 ml.) were added. After 24 hr. under reflux and cooling, excess of phosphorus was filtered off and most of the acetic acid neutralised with 10% sodium hydroxide solution. The solution was extracted with ether (3 × 100 ml.), and the combined extracts were washed with 10% aqueous sodium hydroxide, dried (Na_2SO_4–K_2CO_3), and distilled, giving 1-*bromo*-2-2′-*methylbenzylnaphthalene* (5·8 g., 57%), m. p. 54°, b. p. 163—164°/10^{-4} mm. (Found: Br, 24·8. $C_{18}H_{15}Br$ requires Br, 25·7%).

2-*Benzyl*-1-*bromonaphthalene*.—1-Bromo-2-naphthaldehyde (7 g.) in benzene (30 ml.) and ether (20 ml.) was added to phenylmagnesium bromide (from magnesium, 0·8 g., and bromobenzene, 5 g.) in ether (25 ml.), then treated as above, giving 2-*benzyl*-1-*bromonaphthalene*, m. p. 39—40°, b. p. 136—138°/10^{-4} mm., n_D^{21} 1·6690 (Found: C, 68·6; H, 4·6; Br, 26·5. $C_{17}H_{13}Br$ requires C, 68·7; H, 4·4; Br, 26·9%).

2-*Benzyl*-1-*naphth*[^{14}C]*oic Acid*.—A Grignard reagent was prepared by heating under reflux 2-benzyl-1-bromonaphthalene (1·3 g.), magnesium (0·13 g.), iodine (1 crystal), and methyl iodide (2—3 drops) in ether (20 ml.) for 2 hr. $^{14}CO_2$, generated with concentrated sulphuric acid from barium [^{14}C]carbonate (591 mg., 3 mc) in a closed vacuum-system, was condensed into the Grignard solution by cooling it in liquid nitrogen. Isolation of the acid as for *o*-benzylbenzoic acid (see preceding paper) gave after one crystallisation from *cyclo*hexane plates of 2-*benzyl*-1-*naphth*[^{14}C]*oic acid* (0·66 g., 84%), m. p. 132—133°. A yield of 86% was obtained from a similar experiment. A sample recrystallised to constant m. p. from *cyclo*hexane had m. p. and mixed m. p. 135—137° (Found: C, 82·1; H, 5·4. $C_{15}H_{14}O_2$ requires C, 82·5; H, 5·3%).

1 : 2-[9-^{14}C]*Benzanthracene*.—The above acid (0·66 g.) was dissolved in anhydrous hydrogen fluoride (*ca.* 15 ml.) in a platinum crucible and kept at room temperature for 15 min. with occasional shaking. The orange liquid was poured on ice-water and the 1 : 2-benzanthr-10-one

[12] Hall and Mitchell, *J.*, 1951, 1375; cf. Adams and Binder, *J. Amer. Chem. Soc.*, 1941, **63**, 2773.
[13] Newman and Kosak, *J. Org. Chem.*, 1949, **14**, 375; Hebbelynck and Martin, *Bull. Soc. chim. belges*, 1952, **61**, 635.
[14] Hewett, *J.*, 1940, 293.

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(or mixed isomers [15]) (0·61 g.), m. p. 140—141°, filtered off, dried *in vacuo*, and used without purification. This product (170 mg.) was heated with activated zinc dust (1 g.) in 2N-sodium hydroxide (8 ml.) and toluene (5 ml.) for 5 hr., then allowed to cool. The aqueous layer was extracted with benzene (2 × 5 ml.), and the excess of zinc washed with hot benzene (2 × 5 ml.). The combined solvents and washings were dried (Na_2SO_4) and distilled. The residual solid 1 : 2-[9-^{14}C]benzanthracene crystallised from methanol in plates (140 mg.), m. p. 157—158°, 0·96 mc/mmole; to the mother-liquors was added carrier 1 : 2-benzanthracene (220 mg.), giving on concentration and crystallisation 1 : 2-[9-^{14}C]benzanthracene (250 mg.), m. p. 156—157°, 71·7 μc/mmole (overall radiochemical yield from $^{14}CO_2$ 83%).

2-2′-*Methylbenzyl*-1-*naphth*[^{14}C]*oic Acid*.—Carboxylation of a Grignard reagent from 1-bromo-2-2′-methylbenzylnaphthalene (1·9 g.), magnesium (0·15 g.), iodine (1 crystal), and methyl iodide (2 drops) in ether (20 ml.) with $^{14}CO_2$ (from barium [^{14}C]carbonate, 0·591 g., 3 mc) with stirring at room temperature for 1 hr., gave 2-2′-methylbenzyl-1-naphth[^{14}C]oic acid (0·69 g., 83%), plates (from *cyclo*hexane), m. p. and mixed m. p. 145—146° (Found : C, 82·4; H, 5·5. Calc. for $C_{19}H_{16}O_2$: C, 82·6; H, 5·8%) (Fieser and Newman [16] give m. p. 144—145°).

5-*Methyl*-1 : 2-[9-^{14}C]*benzanthracene*.—The above acid (0·40 g.) was kept in anhydrous hydrogen fluoride (*ca.* 8 ml.) at room temperature for 15 min., then poured on ice-water, and the 5-methyl-1 : 2-benzanthr-10-one (0·39 g.), m. p. 162—163°, filtered off, dried *in vacuo*, and used without purification. It (150 mg.) was heated with activated zinc dust (1 g.) in 2N-sodium hydroxide (8 ml.) and toluene (5 ml.) for 6 hr. Crystallisation of the product from methanol gave 5-methyl-1 : 2-[9-^{14}C]benzanthracene (120 mg.), m. p. 150—152°. This was chromatographed on alumina in benzene, then crystallised from methanol as plates (95 mg.), m. p. 152—153°, 1·1 mc/mmole. The m. p. was undepressed on admixture with an inactive sample of m. p. 151—152° (Fieser and Newman [16] give m. p. 158·5—159·1°) (Found : C, 93·7; H, 5·8. Calc. for $C_{19}H_{14}$: C, 94·2; H, 5·8%).

2-*Benzyltetralone*.—Tetral-1-one (5 g.) and benzyl bromide (6 g.) were added in one lot to a boiling solution of potassium (2·8 g.) in *tert.*-butyl alcohol (30 ml.), heated under reflux for 35 min., allowed to cool, and treated with ice-cold concentrated hydrochloric acid (50 ml.). The solution was ether-extracted, dried (Na_2SO_4), and evaporated under reduced pressure. Distillation of the residue gave tetralone (2 g.) and 2-benzyltetralone (1·8 g.), b. p. 155—159°/10^{-2} mm., m. p. 53—54° [from light petroleum (b. p. 60—80°)] (Borsche *et al.*[17] give m. p. 53—54°).

2-*Benzyl*-1 : 2 : 3 : 4-*tetrahydro*-1-*naphthol*.—2-Benzyltetralone (1·5 g.) in ether (25 ml.) was added to a stirred suspension of lithium aluminium hydride (0·5 g.) in ether (75 ml.), and stirred at room temperature for 1 hr., and excess of hydride decomposed with 2N-sulphuric acid. Isolation with ether gave 2-*benzyl*-1 : 2 : 3 : 4-*tetrahydro*-1-*naphthol* (1·2 g.), plates [from light petroleum (b. p. 60—80°)], m. p. 119—120° (Found : C, 85·6; H, 7·6. $C_{17}H_{18}O$ requires C, 85·7; H, 7·6%).

2-*Benzylidenetetralone*.—Benzaldehyde (7 g.) and tetral-1-one (10 g.) were added in one lot to 5% methanolic potassium hydroxide (80 ml.) at 50°. The solution was allowed to cool overnight, the alkaline solution was neutralised with acetic acid, and the crystals were filtered off. Crystallisation from methanol gave pale yellow needles of 2-benzylidenetetralone (13·5 g.), m. p. 105° (Rapson and Shuttleworth [18] give m. p. 105°).

Reduction of 2-benzylidenetetralone (4 g.) in ether (150 ml.) with lithium aluminium hydride (1·5 g.) under reflux for 60 min. gave a quantitative yield of 2-benzyl-1 : 2 : 3 : 4-tetrahydro-1-naphthol, m. p. and mixed m. p. 119—120°.

2-*Benzyl*-3 : 4-*dihydronaphthalene*.—2-Benzyl-1 : 2 : 3 : 4-tetrahydro-1-naphthol (15 g.) was dissolved in benzene (150 ml.), and phosphorus tribromide (25 g.) and 2—3 drops of pyridine were added. The mixture was heated for 3 hr. at 55°. Next morning the solution was poured on crushed ice, and the organic layer separated, washed with water, and dried (Na_2SO_4). Removal of the solvent under reduced pressure gave an oil. On distillation hydrogen bromide was evolved, giving only 2-*benzyl*-3 : 4-*dihydronaphthalene* (11·5 g.), b. p. 126°/0·1 mm., n_D^{23} 1·6162 (Found : C, 92·1; H, 7·2. $C_{17}H_{14}$ requires C, 92·7; H, 7·3%), $\lambda_{max.}$ 2660 Å (ε 13,600 in EtOH).

[15] Cf. Thomson, *Quart. Rev.*, 1956, **10**, 27.
[16] Fieser and Newman, *J. Amer. Chem. Soc.*, 1936, **58**, 2376.
[17] Borsche, Hofmann, and Kuhn, *Annalen*, 1943, **554**, 23.
[18] Rapson and Shuttleworth, *J.*, 1940, 636.

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2-Benzylnaphthalene.—2-Benzyl-3 : 4-dihydronaphthalene (0·9 g.) and 5% palladium–charcoal (0·3 g.) were heated at 200° for 1 hr., then at 290—300° for 15 min. The products were isolated with hot ethanol and on cooling in carbon dioxide–methanol 2-benzylnaphthalene (0·8 g.) crystallised in plates, m. p. 54—55° (Nenitzescu *et al.*[19] give m. p. 55·5°).

1-2′-Chlorobenzylnaphthalene.—*o*-Chlorobenzaldehyde (42 g.) in ether (150 ml.) and 1-naphthylmagnesium bromide (from magnesium, 8·4 g., and 1-bromonaphthalene, 67·5 g.) in ether (450 ml.) gave a crude alcohol which was heated in glacial acetic acid (750 ml.) with iodine (15 g.), red phosphorus (15 g.), and water (75 ml.) for 27 hr., filtered, treated with ice, and extracted with ether (3 × 100 ml.). The combined extracts were washed several times with 10% aqueous sodium hydroxide, dried (Na_2SO_4–K_2CO_3), and distilled, giving the chloro-compound (47 g.), b. p. 139—140°/0·05 mm. (Bradsher[9] gives b. p. 189—192°/2 mm.).

o-Bromobenzaldehyde similarly gave *1-2′-bromobenzylnaphthalene* (62%), b. p. 150°/10^{-3} mm., n_D^{22} 1·6645 (Found: C, 69·5; H, 4·4; Br, 27·0. $C_{17}H_{13}Br$ requires, C, 68·7; H, 4·4; Br, 26·9%).

1-2′-[^{14}C]Carboxybenzylnaphthalene.—A Grignard reagent, prepared by heating the preceding bromide (3·2 g.) for *ca.* 1 hr., with magnesium (0·35 g.), iodine (1 crystal), and methyl iodide (1—2 drops), in ether (15 ml.), was treated with $^{14}CO_2$ (from barium [^{14}C]carbonate, 1·97 g. 1 mc) and stirred for 30 min. at room temperature, giving the desired acid (80%), which after several crystallisations from *cyclo*hexane had m. p. 144—145° (Bergmann and Loewenthal[20] give m. p. 147°).

An attempt to form a Grignard reagent from the chloro-compound failed even after refluxing in ether or tetrahydrofuran for up to 24 hr.

1 : 2-[10-^{14}C]Benzanthracene.—The foregoing acid (0·5 g.) was kept in anhydrous hydrogen fluoride (*ca.* 5 ml.) at room temperature for 10 min. Isolation of the product as before gave a solid which was heated in acetone (40 ml.) with charcoal, filtered, and cooled slowly to −10°. A product (250 mg.), m. p. 157—158°, was obtained, and on recrystallisation from acetone a product (160 mg.) (*a*), m. p. 157—158°. The solid did not dissolve in cold 10% potassium hydroxide solution but on warming exhibited a strong green fluorescence in ultraviolet light. From the mother-liquors of the crystallisation was obtained a solid (125 mg.) (*b*), m. p. 230—232°, which was not investigated.

The product (*a*) above (135 mg.) was reduced with zinc dust (1 g.) as previously described, giving 1 : 2-[10-^{14}C]benzanthracene (105 mg.), m. p. 153—154°, 104 μc/mmole.

1-Napth[^{14}C]oic Acid.—$^{14}CO_2$ (from barium [^{14}C]carbonate, 1·97 g., 1 mc) was condensed into 1-naphthylmagnesium bromide (from magnesium, 0·3 g., and 1-bromonaphthalene, 3·2 g.) in ether (30 ml.) in a closed vacuum-system. The solution was stirred at room temperature for 1 hr. Isolation as described above gave 1-naphth[^{14}C]oic acid (1·62 g., 94%), m. p. 158—159° (lit.,[21] m. p. 160—161°). The acid was used without purification.

1-Naphthyl[^{14}C]methyl Alcohol.—Labelled 1-naphthoic acid (1·62 g.) was reduced with lithium aluminium hydride (2 g.) in ether (75 ml.). Isolation of the product with ether and crystallisation from *cyclo*hexane gave 1-naphthyl[^{14}C]methyl alcohol (1·2 g., 81%), m. p. 63—64° (Manske and Ledingham[22] gave m. p. 64°).

1-Naphth[^{14}C]aldehyde.—(*a*) 1-Naphthyl[^{14}C]methyl alcohol (1·2 g.) and tetrachloro-1 : 2-benzoquinone (2 g.) in chloroform (50 ml.) were left for 3 days at room temperature. The solution was then chromatographed on alumina in chloroform, and the chloroform eluate distilled under reduced pressure. The residual oil of 1-naphth[^{14}C]aldehyde was used for the next stage. The 2 : 4-dinitrophenylhydrazone, crystallised from ethyl acetate, had m. p. and mixed m. p. 257—258° (decomp.) (lit.,[23] m. p. 254°). The semicarbazone, crystallised from aqueous methanol, had m. p. 215—218° (lit.,[23] 219°). Derivatives were prepared from aldehyde isolated during an inactive run. Yields of derivatives indicated a 62% yield of 1-naphthaldehyde.

(*b*) The alcohol (0·5 g.), in pyridine (5 ml.), was added to chromium trioxide (0·5 g.) in pyridine (5 ml.). Next morning the mixture was poured into water (200 ml.) and ether-extracted. The extract was washed with 2N-hydrochloric acid (2 × 50 ml.), dried (Na_2SO_4), and evaporated

[19] Nenitzescu, Isacescu, and Ionescu, *Annalen*, 1931, **491**, 217.
[20] Bergmann and Loewenthal, *Bull. Soc. chim. France*, 1952, 66.
[21] King, *J. Amer. Chem. Soc.*, 1944, **66**, 894.
[22] Manske and Ledingham, *Canad. J. Res.*, 1939, **17**, 14.
[23] Coles and Dodds, *J. Amer. Chem. Soc.*, 1938, **60**, 853.

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under reduced pressure. The residue was converted into the semicarbazone (0·58 g., 86%), m. p. 215—218°.

1-(α-*Hydroxy*-2-*methylbenzyl*)*naphthalene*.—To 1-naphth[^{14}C]aldehyde (method *a*) was added carrier aldehyde (1 g.) dissolved in ether (25 ml.); the mixture was added dropwise to *o*-tolylmagnesium bromide (from magnesium, 0·4 g., and *o*-bromotoluene, 2·5 g.) in ether (50 ml.). The whole was stirred at room temperature for 30 min. and then treated with excess of saturated aqueous ammonium chloride. Isolation with ether gave the *alcohol* (1·8 g.) which crystallised in plates [from light petroleum (b. p. 60—80°)], m. p. 115°, undepressed on admixture with a non-radioactive sample of m. p. 118—118·5° (Found: C, 87·5; H, 6·4. $C_{18}H_{16}O$ requires C, 87·1; H, 6·4%).

1 : 2-[9-^{14}C]*Benzanthracene*.—The above alcohol (0·5 g.) and zinc dust (0·3 g.) were heated at 400—410° for 3 hr. and, after cooling, extracted with hot light petroleum (b. p. 60—80°) and chromatographed on alumina. Removal of solvent gave 1 : 2-[9-^{14}C]benzanthracene (140 mg.), m. p. 152—154°, which crystallised from methanol in plates (100 mg.), m. p. 156—157°, 35 μc/mmole. The overall radiochemical yield from $^{14}CO_2$ was 6%.

1-*Naphthyl* o-*Tolyl Ketone*.—The preceding alcohol (2 g.) was treated in acetone (50 ml.) with excess of chromic acid in aqueous sulphuric acid.[7] After 5 min. the mixture was diluted with water (300 ml.) and ether-extracted. The ether layer was dried (Na_2SO_4–K_2CO_3) and solvent removed under reduced pressure. The residual crude ketone was heated with zinc dust (0·5 g.) for 2 hr. at 410°. Isolation with light petroleum (b. p. 60—80°) as in the above pyrolysis gave after chromatography 1 : 2-benzanthracene (0·6 g., 33%), m. p. 156—157°.

Metallation of 1-2′-*Chlorobenzylnaphthalene*.—The chloro-compound (3·5 g.) in ether (10 ml.) was added to lithium (0·3 g.) in ether (50 ml.) at −10° to −20°. The solution became green after 3—4 minutes' stirring, and deep crimson after *ca.* 30 min. The solution was stirred for 2 hr., then poured on excess of powdered carbon dioxide and allowed to attain room temperature. Isolation of acidic products as above gave a gum which was dissolved in benzene and precipitated with light petroleum (b. p. 40—60°). Crystallisation from light petroleum gave pale yellow plates (1·8 g.), m. p. 133—134° (Found: C, 81·6; H, 5·6. Calc. for $C_{18}H_{14}O_2$: C, 82·5; H, 5·3%). From the neutral fraction was obtained 1-benzylnaphthalene (0·9 g.) which, crystallised from light petroleum (b. p. 40—60°), had m. p. 54—55°, undepressed on admixture with a sample of m. p. 56—58°.

1 : 2-*Benz*[9-^{14}C]*anthraquinone*.—The crude 1 : 2-benzanthrone (above) (240 mg., *ca.* 1 mc) was dissolved in glacial acetic acid (10 ml.) and heated to boiling. Excess of 30% hydrogen peroxide (6 ml.) was added and the solution heated under reflux for 5 min. The solution was diluted with water (15 ml.). The crude orange quinone (200 mg.), m. p. 157—167°, crystallised. Inactive quinone (500 mg.) was added to the active product and the whole recrystallised from acetic acid, giving the [9-^{14}C]quinone (550 mg.), m. p. 165—166° (*a*). To the mother liquors was added carrier inactive quinone (500 mg.); crystallisation gave a further yield of active quinone (460 mg.), m. p. 165—167° (*b*). A further crop (170 mg.) crystallised overnight [m. p. 165—167° (*c*)] (Badger and Cook [24] give m. p. 163—168°).

9 : 10-*Dimethyl*-1 : 2-[9-^{14}C]*benzanthracene*.—The quinone (720 mg., *a* + *c*) in benzene (5 ml.) was added to methylmagnesium iodide (from magnesium, 1·2 g., and methyl iodide, 8 g.) in ether (15 ml.). After 30 minutes' heating the solution was left for 18 hr. at 2° in nitrogen, then poured at 0° into hydriodic acid (12 ml.; *d* 1·7) in methanol (35 ml.), and glacial acetic acid (35 ml.) was added. The iodomethyl compound slowly separated, was filtered off, dissolved in dioxan (40 ml.) containing concentrated hydrochloric acid (2 ml.), and was added to stannous chloride (8 g.) in dioxan (30 ml.) containing concentrated hydrochloric acid (20 ml.). After 5 min. under reflux, the solution was set aside for 30 min., water (*ca.* 250 ml.) added, and the solution left at 0° for 2—3 hr., giving 9 : 10-dimethyl-1 : 2-[9-^{14}C]benzanthracene (330 mg.), m. p. and mixed m. p. 122—123° (Sandin and Fieser [11] give m. p. 122—123°), 124 μc/mmole. The quinone (460 mg., *b*) gave a hydrocarbon (210 mg.), m. p. 122—123°, 23·5 μc/mmole. The radiochemical yield from crude 1 : 2-benzanthrone was thus 18%.

1 : 2-[9-^{14}C]*Benzanthracene of High Activity*.—1 : 2-[9-^{14}C]Benzanthracene (270 mg., 59%), m. p. 155—156°, 22·2 mc/mmole, was prepared as described above from barium [^{14}C]carbonate (0·394 g., 46 mc). Dilution analysis indicated a radiochemical purity >98%.

Oxidation of 1 : 2-[9-^{14}C]*Benzanthracene*.—The hydrocarbon (120 mg., 11·6 mc) was treated in boiling glacial acetic acid (20 ml.) with 30% hydrogen peroxide (4 ml.) and heated under

[24] Badger and Cook, *J.*, 1939, 804.

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reflux for 5 min., rapidly becoming orange. 1 : 2-Benzanthraquinone (250 mg.) was dissolved in the solution, water (15 ml.) was added, and the solution allowed to cool. 1 : 2-[9-^{14}C]Benzanthraquinone (276 mg.), m. p. 163—165° (*a*), crystallised. To the mother-liquors was added carrier quinone (450 mg.); crystallisation yielded radioactive quinone (427 mg.), m. p. 164—166° (*b*).

9 : 10-*Dimethyl*-1 : 2-[9-^{14}C]*benzanthracene*.—Conversion of the quinone (*a*) into the hydrocarbon as described above gave 9 : 10-dimethyl-1 : 2-[9-^{14}C]benzanthracene (126 mg.), m. p. 122—123°, 2·6 mc/mmole (radiochemical purity by dilution analysis >98%). From quinone (*b*) was obtained hydrocarbon (237 mg.), m. p. 122—123°, 0·71 mc/mmole. The overall radiochemical yield from benzanthracene was thus 18%.

The Reaction of 1 : 2-*Benzanthr*-9-*one with Methylmagnesium Iodide*.—The crude ketone (150 mg.) in benzene (5 ml.) was added to methylmagnesium iodide (from magnesium, 72 mg., and methyl iodide, 430 mg.) in ether (10 ml.) and the mixture heated under reflux for 3 hr. The solution was cooled and excess of hydrochloric acid (50% v/v) added. The aqueous layer was extracted with benzene (2 × 10 ml.). The combined organic layers were dried (Na_2SO_4), and the solvent was removed under reduced pressure. Crystallisation of the residue from acetone–methanol gave a product (60 mg.), m. p. 237—239° (Found: C, 87·9; H, 4·5. Calc. for $C_{18}H_{12}O$: C, 88·5; H, 4·9%), which is probably the starting ketone or its tautomer. No fluorescent hydrocarbons were obtained.

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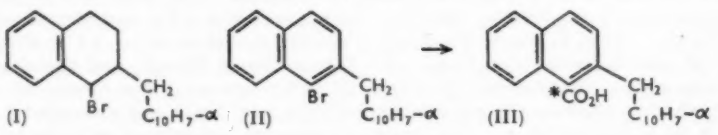
539. ^{14}C-*Labelled Polycyclic Aromatic Hydrocarbons. Part III.*[1] *The Synthesis of* 1 : 2-5 : 6-[9-^{14}C]*Dibenzanthracene.*

By J. R. CATCH and E. A. EVANS.

1 : 2-5 : 6-[9-^{14}C]Dibenzanthracene has been synthesised in three radioactive stages from $^{14}CO_2$, the overall yield being 30%.

THIS paper records a synthesis of 1 : 2-5 : 6-dibenzanthracene in three radioactive stages from $^{14}CO_2$, in about 30% overall yield, which, although lower than in the tri- and tetracyclic series, is better than was obtained by Heidelberger and his collaborators.[2]

The bromo-compound (I) was prepared by condensing 1-naphthaldehyde with tetral-1-one, reducing the naphthylidene compound with lithium aluminium hydride, and treating the resulting saturated alcohol with phosphorus tribromide. 1-Bromo-1 : 2 : 3 : 4-tetrahydro-2-1′-naphthylmethylnaphthalene (I) however did not react with magnesium, and could not be cross-metallated with *n*-butyl-lithium, perhaps owing to dehydrobromination (cf. Part II). 1-Bromo-2-1′-naphthylmethylnaphthalene (II) was prepared by treating



1-bromo-2-naphthaldehyde with 1-naphthylmagnesium bromide and reducing the secondary alcohol with red phosphorus and iodine. This bromide had to be purified by chromatography before it would form a Grignard reagent, but impure bromide could be cross-metallated with *n*-butyl-lithium and on carboxylation gave 2-1′-naphthylmethyl-1-naphthoic acid (III) in 67% yield based on $^{14}CO_2$: carboxylation of the Grignard reagent gave 83—98% yields. The acid was cyclised with anhydrous hydrogen fluoride and the product reduced to 1 : 2-5 : 6-dibenzanthracene with zinc dust in sodium hydroxide. The overall radiochemical yield was 31%.

[1] Part II, preceding paper.
[2] Heidelberger, Brewer, and Dauben, *J. Amer. Chem. Soc.*, 1947, **69**, 1390.

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Cyclisation of the acid was less complete than in the previous cases (Parts I and II); use of concentrated sulphuric acid followed by reduction failed to yield dibenzanthracene.

(IV) 2 : 1-$C_{10}H_6Me{\cdot}CO{\cdot}C_{10}H_7$-α 2 : 1-$C_{10}H_6Me{\cdot}CO{\cdot}C_{10}H_7$-β (V)

In another attempted route the ketones (IV and V) were prepared from 1- and 2-naphthaldehyde respectively with 2-methyl-1-naphthylmagnesium bromide, the secondary alcohol being oxidised with chromic acid in aqueous sulphuric acid.[3] Pyrolysis of either ketone at *ca.* 500° gave only traces of fluorescent gums on a small scale (*viz.*, *ca.* 200 mg.) although up to 33% yield of dibenzanthracene has been obtained in larger-scale experiments.[4] 2-Naphth[^{14}C]aldehyde was prepared in 81% yield by oxidation of 2-naphthyl-[^{14}C]methyl alcohol with tetrachloro-1 : 2-benzoquinone.[1, 5]

The radiochemical purities of the hydrocarbons described in this and the preceding papers were determined by dilution analysis, *viz.*, by dilution of the active material with pure carrier inactive material, homogenising the whole in a suitable solvent, and evaporating the solution to dryness. The residue is assayed (result *A*) in the usual manner, then crystallised and assayed again (result *B*). *B*/*A* gives a measure of the radiochemical purity.

The 1 : 2-5 : 6-[9-^{14}C]dibenzanthracene prepared from the acid (III) had the same ultraviolet absorption spectrum as the carrier hydrocarbon, but although the melting point (261—262°) was also the same it contained *ca.* 10% of a radioactive impurity which was removed only by crystallisation from benzene; chromatography on alumina in benzene and sublimation were only partially successful. After crystallisation the radiochemical purity was >95%.

The method of assay of the radioactive dibenzanthracene adopted by Heidelberger *et al.*[2] would not indicate the radiochemical purity of the product.

Experimental

For general methods see Part I. Ultraviolet absorptions refer to ethanol solutions and were measured with a Unicam S.P. 500 instrument.

1-*Naphthylmethyl Alcohol*.—1-Naphthaldehyde (25 g.) in anhydrous ether (25 ml.) was added dropwise to a stirred suspension of lithium aluminium hydride (5 g.) in ether (300 ml.) at room temperature. Excess of lithium aluminium hydride was decomposed with water, and excess of sulphuric acid (25% v/v) added. The ether layer was dried (Na_2SO_4–K_2CO_3) and the solvent removed under reduced pressure, giving 1-naphthylmethyl alcohol (22 g.) which crystallised in plates (from benzene–*cyclo*hexane), m. p. 63—64° (Manske and Ledingham [6] gave m. p. 64°). Similar reduction of 1-naphthoic acid gave a quantitative yield of 1-naphthylmethyl alcohol, m. p. 64°.

1-*Bromomethylnaphthalene*.—The alcohol (18 g.) was heated in benzene (150 ml.) with phosphorus tribromide (9·5 ml.) and pyridine (2—3 drops) at 55° for 2 hr., then treated with ice. The organic layer was washed with water, 2N-sodium hydrogen carbonate and saturated salt solution. After drying (Na_2SO_4) the solvent was removed under reduced pressure and the residual oil crystallised from light petroleum (b. p. 40—60°), giving 1-bromomethylnaphthalene (18 g.), m. p. 54—55° (Szmuszkovicz and Bergmann [7] give m. p. 54—55·5°). A lower yield was obtained by the action of *N*-bromosuccinimide on 1-methylnaphthalene as described by Buu-Hoï.[8]

1-*Bromo*-2-1′-*naphthylmethylnaphthalene*.—1-Bromo-2-naphthaldehyde (14 g.) in benzene (100 ml.) was added to 1-naphthylmagnesium bromide (from magnesium, 1·6 g., and 1-bromonaphthalene, 13 g.) in ether (100 ml.), and the mixture heated under reflux for 5 hr. The solution was treated with excess of saturated ammonium chloride, and the organic layer

[3] Cf. Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548.
[4] Fieser, "Organic Reactions," John Wiley & Sons, New York, 1942, Vol. I, p. 151.
[5] Braude, Linstead, and Wooldridge, *J.*, 1956, 3070.
[6] Manske and Ledingham, *Canad. J. Res.*, 1939, **17**, 14.
[7] Szmuszkovicz and Bergmann, *J. Amer. Chem. Soc.*, 1953, **75**, 353.
[8] Buu-Hoï, *J.*, 1946, 830.

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separated. Most of the solvent was distilled off under reduced pressure and the residue heated in glacial acetic acid (150 ml.) with phosphorus (3 g.), iodine (3 g.), and water (25 ml.) for 24 hr. After cooling, excess of red phosphorus was filtered off and most of the acetic acid neutralised with 10% sodium hydroxide solution. The solution was extracted with ether (3 × 100 ml.), and the extracts were washed with 10% aqueous sodium hydroxide and dried (Na_2SO_4–K_2CO_3). The ether was distilled under reduced pressure and the residual dark red oil repeatedly extracted with hot light petroleum (b. p. 40—60°) (total 500 ml.) and chromatographed on alumina in the same solvent. Removal of the solvent gave prisms (10 g.), m. p. 96—97°. Crystallisation from light petroleum (b. p. 40—60°) gave *1-bromo-2-1′-naphthylmethylnaphthalene*, m. p. 96—97° (Found: C, 72·6; H, 4·4; Br, 22·6. $C_{21}H_{15}Br$ requires C, 72·7; H, 4·3; Br, 23·0%).

2-1′-Naphthylmethyl-1-naphth[^{14}C]*oic Acid.*—(a) *Grignard method.* A Grignard reagent was prepared from 1-bromo-2-1′-naphthylmethylnaphthalene (1·5 g.), magnesium (0·13 g.), iodine (1 crystal), and methyl iodide (1—2 drops) in ether (20 ml.) under reflux in 2—3 hr. $^{14}CO_2$ (generated from barium [^{14}C]carbonate, 0·394 g., 46 mc, with concentrated sulphuric acid) was condensed into the above Grignard reagent in a closed vacuum-system by freezing in liquid nitrogen. Working up the product as before (see Part I) gave the *acid* which crystallised from benzene–*cyclo*hexane (yield 0·613 g., 98%) and had m. p. 191—192°, undepressed on admixture with a non-radioactive sample (Found: C, 84·2; H, 5·2. $C_{22}H_{16}O_2$ requires C, 84·6; H, 5·3%). In other experiments yields of 83% and 92% were obtained.

(b) *Cross-metallation.* 1-Bromo-2-1′-naphthylmethylnaphthalene (1·7 g.) in ether (5 ml.) was added to *n*-butyl-lithium (from lithium, 0·07 g., and *n*-butyl bromide, 1 g.) in ether (20 ml.) at −20°. The solution was stirred for 1½ hr. at room temperature. $^{14}CO_2$ (from barium carbonate, 0·591 g., 1 mc) was condensed into the solution. After 30 minutes' stirring at room temperature the solution was left overnight and worked up as before. Crystallised from *cyclo*hexane–benzene, the acid (0·6 g., 67%) had m. p. 190—192°.

1 : 2-5 : 6-[*9-*^{14}C]*Dibenzanthracene.*—(*a*) The acid (0·5 g., from method *b*; *ca.* 0·3 mc/mmole) was left in anhydrous hydrogen fluoride (10—15 ml.) for 30 min. at room temp., then poured on ice. The product was filtered off and heated under reflux for *ca.* 7 hr. with zinc dust (3 g.), 2N-sodium hydroxide (20 ml.), and toluene (15 ml.). Working up as described for 1 : 2-benzanthracene (Part II) gave 1 : 2 : 5 : 6-dibenzanthracene which, crystallised from benzene, had m. p. and mixed m. p. 258—260° (230 mg., 55% based on acid). This material was slightly brown but on chromatography on alumina in benzene, and then crystallisation from benzene formed colourless plates (110 mg.), m. p. 261—262°, 0·3 mc/mmole. To the mother-liquors of the crystallisation was added carrier dibenzanthracene (50 mg.) and the solution was concentrated, yielding 1 : 2 : 5 : 6-dibenzanthracene (62 mg.), m. p. 259—261°, 176 μc/mmole. This represents a total radiochemical yield of 32% (158 μc) based on acid (the acid recovered was taken into account in determining yields).

A small quantity (50 mg.) of unchanged acid, m. p. and mixed m. p. 191—192°, was isolated from the alkaline layer of the reduction by acidification and ether-extraction.

(*b*) The acid (0·575 g., 46 mc) was converted into dibenzanthracene as described above. The crude product (150 mg.), m. p. 230—250°, was chromatographed on alumina in benzene and then crystallised from benzene–methanol, yielding almost colourless plates of [*9-*^{14}C]dibenzanthracene (120 mg., 35% from acid), m. p. 259—261° (radiochemical purity at this stage by dilution of a rechromatographed sample, m. p. 261—262°, was 90%). Carrier dibenzanthracene (*ca.* 150 mg.) was added to the above, and the whole crystallised from benzene, yielding [*9-*^{14}C]dibenzanthracene (168 mg.), m. p. 261—262°, 10·5 mc/mmole (dilution analysis indicated a radiochemical purity >95%). To the mother-liquors of the crystallisation was added carrier dibenzanthracene and a further 3 mc of active hydrocarbon were isolated (m. p. 261—262°). The product had absorption max. at 2220 (ε 54,000), 2310 (ε 27,300), 2780 (ε 40,700), 2860 and 2880 (ε 82,400), 2970 (ε 143,000), 3200 (ε 16,400), 3320 (ε 13,900), 3490 (ε 12,600), 3750 (ε 200) and 3930 Å (ε 700). The same maxima and intensity were found with the dibenzanthracene of 90% radiochemical purity. From the aqueous alkaline layer of the reduction was recovered starting acid (190 mg.), m. p. and mixed m. p. 189—192°.

2-1′-Naphthylmethyltetralone.—Tetral-1-one (12 g.) in toluene (15 ml.) was added under nitrogen to a suspension of sodamide (3·3 g.) in toluene (80 ml.) and the mixture heated under reflux for 6 hr. After cooling, 1-bromomethylnaphthalene (16·5 g.) in toluene (25 ml.) was added and the mixture cautiously heated. When the vigorous reaction had subsided the mass was refluxed for 6 hr. and then treated with water and excess of 25% sulphuric acid. The aqueous

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layer was extracted with ether (2 × 50 ml.). The combined extracts were washed with water (100 ml.) and saturated salt solution (50 ml.) and dried (Na_2SO_4). The solvents were distilled under reduced pressure and the residue distilled, giving unchanged tetralone (4 g.), b. p. 74°/5 mm., and the product (10·5 g.), b. p. 188—192°/10^{-2} mm., which crystallised from methanol in prisms, m. p. 92—93° (7·5 g.) (Szmuszkovicz and Bergmann [7] give m. p. 92—93°).

1 : 2 : 3 : 4-*Tetrahydro*-2-1′-*naphthylmethyl*-1-*naphthol*.—The foregoing ketone (6 g.) in anhydrous ether (100 ml.) was heated with lithium aluminium hydride (2 g.) in ether (200 ml.) for 15 min., then stirred for 1 hr. at room temperature. Isolation with ether gave the alcohol (6 g.) which, crystallised from aqueous methanol, had m. p. 112—114°, $\lambda_{max.}$ 2740 (ε 6900), 2830 (ε 8000), 2950 (ε 5500), 3140 Å (ε 500).

Condensation of Tetral-1-*one and* 1-*Naphthaldehyde*.—Tetral-1-one (19 g.) and 1-naphthaldehyde (21·5 g.) were added in one lot to 10% methanolic potassium hydroxide (250 ml.) at 60—65° and left for 1 day at room temperature. The solution was neutralised with glacial acetic acid and the solid filtered off and crystallised from methanol, giving pale yellow needles of 2-1′-naphthylidenetetralone (35 g., 95%), m. p. 131—132° (Buu-Hoï and Cagniant [9] give m. p. 131°), $\lambda_{max.}$ 2680 Å (ε 23,000). The m. p. was not raised by chromatography on alumina in benzene.

1 : 2 : 3 : 4-*Tetrahydro*-2-1′-*naphthylmethyl*-1-*naphthol*.—The preceding tetralone (15 g.) was stirred in anhydrous ether (500 ml.) with lithium aluminium hydride (3 g.) under reflux for 2 hr. Next morning water and excess of 25% sulphuric acid were added, the products isolated with ether and dried (Na_2SO_4–K_2CO_3), and the solvents distilled off. The residual solid crystallised from aqueous ethanol, giving a quantitative yield of the *tetrahydronaphthol*, m. p. and mixed m. p. 114° (Found: C, 87·3; H, 7·2. $C_{21}H_{20}O$ requires C, 87·3; H, 6·9%), $\lambda_{max.}$ 2740 (ε 6400), 2830 (ε 7200), 2950 Å (ε 5000). The alcohol was recovered unchanged after being shaken for 6 hr. with hydrogen and platinic oxide in ethanol or acetic acid.

1-*Bromo*-1 : 2 : 3 : 4-*tetrahydro*-2-1′-*naphthylmethylnaphthalene*.—The tetrahydronaphthol (3 g.) was heated in benzene (25 ml.) with phosphorus tribromide (1·5 ml.) and pyridine (1 drop) at 55° for 2 hr., then poured on ice. The organic layer was separated, washed with water and 2N-sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated under reduced pressure, giving the *bromide* (2·1 g.), m. p. 108—109° (decomp.) [from light petroleum (b. p. 60—80°)] (Found: Br, 23·0. $C_{21}H_{19}Br$ requires Br, 22·8%).

The alcohol (1·02 g.) in acetone (25 ml.) was treated with a slight excess of chromic acid in aqueous sulphuric acid [3] at room temperature. Water (50 ml.) was added and the products were isolated with ether giving the ketone (1 g.), m. p. and mixed m. p. 90—92°.

2-*Methyl*-1-*naphthyl* 1-*Naphthyl Ketone* (IV).—1-Naphthaldehyde (7 g.) in ether (25 ml.) was added dropwise to 2-methyl-1-naphthylmagnesium bromide (from magnesium, 1·5 g., and 1-bromo-2-methylnaphthalene, 11 g.), in ether (100 ml.). The solution was stirred for 1 hr., then treated with excess of saturated aqueous ammonium chloride. The ether layer was dried (Na_2SO_4) and the residue, after removal of solvent, was dissolved in acetone (500 ml.) and treated with a slight excess of chromic acid in aqueous sulphuric acid.[3] Water (*ca.* 50 ml.) was added and most of the acetone distilled off under reduced pressure. The residue was poured into water (300 ml.), and the red solid which separated crystallised from ethanol (pale yellow plates, 10 g., 75%). A sample crystallised to constant m. p. had m. p. 169—170° (Found: C, 89·1; H, 5·3. Calc. for $C_{22}H_{16}O$: C, 89·2; H, 5·4%) (Fieser and Dietz [10] give m. p. 171°).

Pyrolysis. The ketone (0·4 g.) was heated for 3 hr. at *ca.* 500°. The products were extracted with hot benzene and chromatographed on alumina in benzene. Removal of the solvent gave 1 : 2 : 5 : 6-dibenzanthracene (25 mg.) which crystallised from benzene in plates, m. p. and mixed m. p. 261—262°. Heating for 5 hr. gave 30 mg. of the hydrocarbon.

2-*Naphth*[^{14}C]*aldehyde*.—2-Naphthyl[^{14}C]methyl alcohol (350 mg.) (tracer level activity, *ca.* 30 μc/mmole), prepared from 2-naphth[^{14}C]oic acid by reduction with lithium aluminium hydride, was dissolved in chloroform (10 ml.), and tetrachloro-1 : 2-benzoquinone (500 mg.) added. The mixture was left for 3 days at room temperature and then chromatographed on alumina in chloroform. Distillation of the eluate gave a solid (320 mg.) which crystallised from light petroleum (b. p. 40—60°) giving 2-naphth[^{14}C]aldehyde (280 mg., 81%), m. p. 62—63° (lit.,[11] m. p. 57—58°).

[9] Buu-Hoï and Cagniant, *Rev. Sci.*, 1942, **80**, 384.
[10] Fieser and Dietz, *Ber.*, 1929, **62**, 1829.
[11] Williams, *Org. Synth.*, 1943, **23**, 63.

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2-Methyl-1-naphthyl 2-Naphthyl Ketone (V).—2-Naphthaldehyde (3·5 g.) in ether (25 ml.) was added to 2-methyl-1-naphthylmagnesium bromide (from magnesium, 0·8 g.) in ether (100 ml.). Working up as for ketone (IV) gave ketone (V) (4·3 g., 65%; m. p. 133—136°), which crystallised from ethanol in pale yellow needles (3·5 g.), m. p. 138—139° (Fieser and Dietz [10] give m. p. 142—143°).

The ketone (160 mg.), m. p. 134—136°, 28 μc/mmole, was obtained from 2-naphth-[^{14}C]aldehyde (240 mg.).

Pyrolysis. Pyrolysis of the ketone (200 mg.) at *ca.* 430° for 3·5 hr. gave only traces of fluorescent gums after chromatography on alumina in benzene.

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540. *Addition of Free Radicals to Unsaturated Systems. Part XIV.* The Direction of Radical Addition to Trifluoroethylene.*

By R. N. HASZELDINE and B. R. STEELE.

Radical attack on trifluoroethylene is 80% on the CHF group and 20% on the CF_2 group; attack by an atom is 60% on the CHF group and 40% on the CF_2 group. This is the first time that anything other than exclusive radical attack on one carbon of an unsymmetrical olefin has been reported. Polytrifluoroethylene thus contains units such as $-CHF{\cdot}CF_2{\cdot}CHF{\cdot}CF_2-$, $-CHF{\cdot}CF_2{\cdot}CF_2{\cdot}CHF-$, and $-CF_2{\cdot}CHF{\cdot}CHF{\cdot}CF_2-$; each unit is flanked by itself or by one of the other units, and the last of these units in particular explains why the polymer is thermally less stable than poly-1 : 1-difluoroethylene. Proofs of structure are given for the reaction products from trifluoroiodomethane and trifluoroethylene, and for those from hydrogen bromide and trifluoroethylene. (*cis* + *trans*)-1 : 2-Difluoroethylene has been prepared. Comments are made on earlier reports on the direction of radical addition to trifluoroethylene.

IT was pointed out earlier [1] that the order of free-radical stability is, in general, primary $-CH_2{\cdot} <$ secondary $>CH{\cdot} <$ tertiary $\geqslant C{\cdot}$ where the terms primary, secondary, and tertiary refer not to the carbon skeleton but to the number of atoms or groups other than hydrogen attached to the carbon atom formally carrying the lone electron. Use of this simple rule enables clear predictions to be made for the direction of addition of an atom or radical to a wide variety of olefins [2] of the type $CH_2{:}CHX$, $R{\cdot}CH{:}CX_2$, $CH_2{:}CX_2$, $CHX{:}CX_2$, $R{\cdot}CX{:}CHX$, $R{\cdot}CX{:}CHR'$, etc., by consideration of the relative stabilities of the possible free-radical intermediates. The rule is of widespread application, but as was pointed out earlier [1] there might be certain secondary free radicals which would be more stable than certain tertiary free radicals; such a situation could arise when the secondary radical contains atoms (*e.g.*, Cl or Br) or groups (*e.g.*, aryl, carboxyl, nitrile) which have a powerful stabilising effect on the radical, whereas the tertiary radical under consideration has atoms (*e.g.*, F) or groups (*e.g.*, alkyl, perfluoroalkyl) which have a relatively weak stabilising effect on a radical. In such special circumstances there will be some overlap between the two classes of radical, and we have therefore sought for examples. A clear-cut example was chloro-1 : 1-difluoroethylene [2] where radical or atom attack is exclusively on the CF_2 group, *i.e.*, stability of $R{\cdot}CF_2{\cdot}CHCl{\cdot}$ > stability of $R{\cdot}CHCl{\cdot}CF_2{\cdot}$.

The stabilising power of fluorine in this connection is only weak, and the direction of atomic and radical addition to trifluoroethylene was therefore examined, since here there was a possibility that the two possible radicals $R{\cdot}CHF{\cdot}CF_2{\cdot}$ and $R{\cdot}CF_2{\cdot}CHF{\cdot}$ would have an approximately equal stability, with the first somewhat more stable than the second. It

* Part XIII, *J.*, 1957, 2193.

[1] Haszeldine, *J.*, 1953, 3565, 3761.

[2] Part XIII, where references to preceding papers are given.

was thus expected that a mixture would arise by free-radical addition, and this is as found experimentally with the trifluoromethyl radical or the bromine atom as the attacking entities. Radical attack is approximately 80% on the CHF group and 20% on the CF_2 group, and atomic attack is approximately 60% on the CHF group and 40% on the CF_2 group. This is the first time that anything other than exclusive or predominant (>95%) radical or atomic attack on one carbon of an unsymmetrical olefin has been reported. The homopolymer of trifluoroethylene thus contains both head to head, and tail to tail units, *e.g.*, $^-CHF{\cdot}CF_2{\cdot}CF_2{\cdot}CHF{\cdot}CHF{\cdot}CF_2{}^-$.

Trifluoroiodomethane and trifluoroethylene do not react in the dark, but when irradiated with light of wavelength >3000 Å give high yields of the monoaddition product $CF_3{\cdot}[C_2HF_3]{\cdot}I$. The reaction is faster in silica vessels, which transmit light of wavelength >2200 Å, and if an excess of trifluoroiodomethane is used the product is again mainly $CF_3{\cdot}[C_2HF_3]{\cdot}I$. Use of an excess of trifluoroethylene leads to the formation of polymer $CF_3{\cdot}[C_2HF_3]_n{\cdot}I$ where $n = 2, 3, 4 \ldots$ etc., as noted for the reaction between trifluoroiodomethane and tetrafluoroethylene.[1] Trifluoroethylene is a reactive olefin in this sense, but less so than tetrafluoroethylene, and it is thus easier to control the chain propagation step:

$$CF_3{\cdot} + CHF{:}CF_2 \longrightarrow CF_3{\cdot}[C_2HF_3]{\cdot} \quad \text{Initiation}$$
$$CF_3{\cdot}[C_2HF_3]{\cdot} + CHF{:}CF_2 \longrightarrow CF_3{\cdot}[C_2HF_3]_n{\cdot} \quad \text{Propagation}$$
$$CF_3{\cdot}[C_2HF_3]_n{\cdot} + CF_3I \longrightarrow CF_3{\cdot}[C_2HF_3]_n{\cdot}I + CF_3{\cdot} \quad \text{Transfer}$$

The monoaddition product can be prepared in 85% yield; that it contains both 1 : 1 : 1 : 2 : 3 : 3- (I) (80%) and 1 : 1 : 1 : 2 : 2 : 3-hexafluoro-3-iodopropane (II) (20%) was shown as follows.

Photochemical chlorination of the monoaddition product under conditions chosen to effect replacement of hydrogen as well as of iodine by chlorine gave a mixture of the two dichlorides[3] 1 : 2- (III) and 1 : 1-dichlorohexafluoropropane (IV). These cannot be

$CF_3{\cdot}CHF{\cdot}CF_2I$	$CF_3{\cdot}CF_2{\cdot}CHFI$	$CF_3{\cdot}CFCl{\cdot}CF_2Cl$	$CF_3{\cdot}CF_2{\cdot}CFCl_2$
(I)	(II)	(III)	(IV)

separated easily by distillation, but can be detected readily by means of their infrared spectra. Compound (III) was prepared for comparison by the reaction of hexafluoropropene with chlorine, and (IV) is the product obtained earlier[3] by the action of chlorine on the reaction product from trifluoroiodomethane with chlorotrifluoroethylene:

$$CF_3I + CF_2{:}CFCl \longrightarrow CF_3{\cdot}CF_2{\cdot}CFClI \xrightarrow{Cl_2} CF_3{\cdot}CF_2{\cdot}CFCl_2$$

It has also been prepared by the sequence

$$C_2F_5{\cdot}CH_2{\cdot}OTs \xrightarrow{KF} C_2F_5{\cdot}CH_2F \xrightarrow{Cl_2} C_2F_5{\cdot}CFCl_2$$
$$(Ts = p\text{-}C_6H_4Me{\cdot}SO_2)$$

The dichlorides react differently on controlled treatment with zinc and ethanol: (III) gives hexafluoropropene, and (IV) gives 1-chloro-1 : 2 : 2 : 3 : 3 : 3-hexafluoropropane (V), both in high yield (*ca.* 85%). The olefin (b. p. −29°) and the reduction product (V) (b. p. 20°)[3] are readily separated by distillation, so the zinc–ethanol reaction provides a means of determining the amounts of (III) and (IV) in a mixture.

The formation of a mixture of (I) and (II) was confirmed by treatment of the mixture

$CF_3{\cdot}CF_2{\cdot}CHFCl$	$CF_3{\cdot}CHF{\cdot}CF_2Br$	$CF_3{\cdot}CF_2{\cdot}CHFBr$
(V)	(VI)	(VII)

with bromine under conditions such that only iodine is replaced by bromine. 1-Bromo-1 : 1 : 2 : 3 : 3 : 3- (VI) and 1-bromo-1 : 2 : 2 : 3 : 3 : 3-hexafluoropropane (VII) were thus obtained. A sample of the former was available from the reaction of hydrogen bromide

[3] Haszeldine and Steele, *J.*, 1953, 1592.

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with hexafluoropropene,[4] a reaction which cannot yield (VII). Infrared spectroscopy of the mixed bromo-compounds prepared from $CF_3{\cdot}[C_2HF_3]{\cdot}I$ revealed the extra bands caused by (VII), a sample of which was synthesised by bromination of 1 : 1 : 1 : 2 : 2 : 3-hexafluoropropane.

Trifluoroethylene does not react with hydrogen bromide in the dark, even at 100° or in the presence of a solvent such as acetic acid; reaction involving ionic intermediates is thus slow. Photochemical reaction

$$Br\cdot + CHF{:}CF_2 \longrightarrow C_2HBrF_3\cdot \xrightarrow{HBr} C_2H_2BrF_3$$

is rapid at room temperature and gives the monoaddition product $H{\cdot}[C_2HF_3]{\cdot}Br$, which has been shown to be a mixture of the two possible isomers (VIII) and (IX). These isomers differ in boiling point by 15° and on a larger scale can be separated by distillation. On a smaller scale, reaction of the mixture with zinc and ethanol gave (*cis* + *trans*)-1 : 2-di-

$CHFBr{\cdot}CHF_2$	$CF_2Br{\cdot}CH_2F$	$CF_2Br{\cdot}CH_2I$	$CF_3{\cdot}CH_2F$
(VIII)	(IX)	(X)	(XI)

fluoroethylene (from VIII) and 1 : 1-difluoroethylene (from IX) in amounts showing that attack by the bromine atom had occurred on the CHF group of trifluoroethylene to an extent of 58% and on the CF_2 group to an extent of 42%. This ratio was substantially unaffected by use of light of wavelength >3000 Å instead of >2200 Å to initiate the reaction.

It was shown earlier [5] that 1-bromo-1 : 1-difluoro-2-iodoethane (X) with mercurous fluoride gives exclusively 1 : 1 : 1-trifluoro-2-iodoethane, and it might have been expected that (IX) would similarly yield 1 : 1 : 1 : 2-trifluoroethane (XI) more rapidly than (VIII) would yield 1 : 1 : 2 : 2-tetrafluoroethane. Examination of infrared spectra showed that preferential replacement of the bromine in (IX) was occurring, but since replacement did not occur exclusively with one of the isomers, this method for determination of the relative proportions of the isomers in $H{\cdot}[C_2HF_3{\cdot}]Br$ was unsatisfactory.

When taken in conjunction with the evidence derived from the trifluoroiodomethane reaction, it is clear that the formation of a mixture of isomers by photochemical reaction of hydrogen bromide with trifluoroethylene provides strong evidence that atomic attack occurs on both the CHF and the CF_2 group, and the possibility of a concurrent ionic reaction ($\overset{\delta-}{C}HF{=}\overset{\delta+}{C}F_2 \longrightarrow CH_2F{\cdot}CF_2Br$) can be neglected.

The direction of ionic attack on trifluoroethylene is shown by its reaction with iodine monochloride to give only 1-chloro-1 : 1 : 2-trifluoro-2-iodoethane (XII). The absence of the other isomer (XIII) was shown by comparison of the infrared spectrum of the product with that of an authentic sample of 1-chloro-1 : 2 : 2-trifluoro-2-iodoethane prepared by reaction of hydrogen iodide with chlorotrifluoroethylene; this last reaction could not produce (XII). The presence of (XIII) in amounts greater than 5% would have been detected spectroscopically. Hydrogen chloride reacts with trifluoroethylene only at 240°

$CF_2Cl{\cdot}CHFI$	$CF_2I{\cdot}CHFCl$	$CF_2Cl{\cdot}CH_2F$	$CHF_2{\cdot}CHFCl$
(XII)	(XIII)	(XIV)	(XV)

in absence of a catalyst to give 1-chloro-1 : 1 : 2-trifluoroethane (XIV), b. p. 12°. Its known isomer 1-chloro-1 : 2 : 2-trifluoroethane (XV) has b. p. 17°. Zinc and ethanol convert (XIV) into 1 : 1-difluoroethylene; under similar conditions (XV) would be reduced or would yield 1 : 2-difluoroethylene. The identification of the products from trifluoroethylene and iodine monochloride or hydrogen chloride thus shows that reactions of this olefin involving ionic intermediates give only one product, whereas radical addition gives two.

[4] Haszeldine, *J.*, 1953, 3559.
[5] Haszeldine and Steele, *J.*, 1954, 923.

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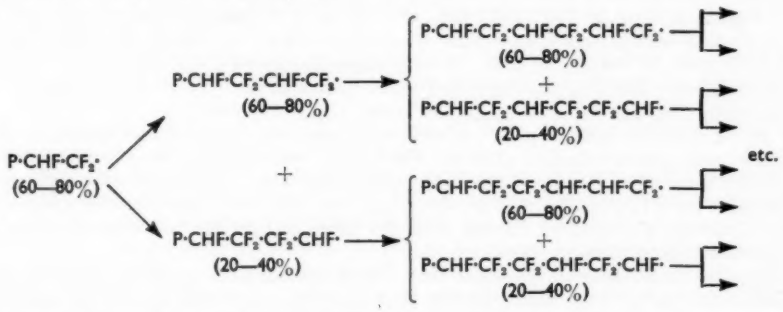
Tarrant and Lilyquist [6] concluded recently that reaction of 1 : 2-dibromo-1-chlorotrifluoroethane with trifluoroethylene gave the compound $CF_2Br{\cdot}CFCl{\cdot}CHF{\cdot}CF_2Br$, since hydrogen bromide could be removed from the product to give olefins. 1 : 2-Dichloro-1-iodotrifluoroethane was similarly considered [6] to give the compound $CF_2Cl{\cdot}CFCl{\cdot}CHF{\cdot}CF_2I$ since dehydroiodination gave the known 3 : 4-dichlorohexafluorobut-1-ene, which in turn yielded hexafluorobuta-1 : 3-diene (40%) on dehalogenation.

Tarrant, Lovelace, and Lilyquist [7] reported that dibromodifluoromethane and trifluoroethylene gave the compounds $CF_2Br{\cdot}CHF{\cdot}CF_2Br$ and $CF_2Br{\cdot}[CHF{\cdot}CF_2]_2{\cdot}Br$ since the dibromopropane gave 3-bromopentafluoroprop-1-ene in 59% yield by reaction with aqueous potassium hydroxide. The evidence presented is clearly insufficient to show that only one isomer is produced during these free-radical reactions, and the possibility of the other isomer's being present was ignored. It is most unlikely that the $CF_2Br{\cdot}CFCl{\cdot}$, $CF_2Cl{\cdot}CFCl{\cdot}$, or $CF_2Br{\cdot}$ radicals would react at all differently from the $CF_3{\cdot}$ radical or the bromine atom as far as attack on trifluoroethylene is concerned, particularly since it has already been shown [3,8] that the $CF_3{\cdot}$ and the $CF_2Cl{\cdot}CFCl{\cdot}$ radical are closely similar in their attack on chlorotrifluoroethylene. The products reported by the above authors are thus not pure compounds but mixtures of $R{\cdot}CHF{\cdot}CF_2X$ (*ca.* 80%) and $RCF_2{\cdot}CHFX$ (*ca.* 20%), and of $R{\cdot}CHF{\cdot}CF_2{\cdot}CHF{\cdot}CF_2X$ (*ca.* 64%), $R{\cdot}CHF{\cdot}CF_2{\cdot}CF_2{\cdot}CHFX$ (*ca.* 16%), $R{\cdot}CF_2{\cdot}CHF{\cdot}CF_2{\cdot}CHFX$ (*ca.* 4%), and $R{\cdot}CF_2{\cdot}CHF{\cdot}CHF{\cdot}CF_2X$ (*ca.* 16%), where R = $CF_2Br{\cdot}CFCl$, $CF_2Cl{\cdot}CFCl$, or CF_2Br, and X = Br or I.

Polytrifluoroethylene.—Homopolymerisation of trifluoroethylene initiated by a free radical P will give both $P{\cdot}CHF{\cdot}CF_2{\cdot}$ (60—80%) and $P{\cdot}CF_2{\cdot}CHF{\cdot}$ (20—40%). The subsequent growth of these radicals by combination with further molecules of trifluoroethylene can be represented as follows :



with a similar sequence initiated by radical $P{\cdot}CF_2{\cdot}CHF{\cdot}$.

The decreasing order of thermal stability for fluoro-polymers is polytetrafluoroethylene > poly-1 : 1-difluoroethylene > polytrifluoroethylene > polyethylene > polyvinyl fluoride.[9] It is known that compounds which contain only one fluorine on a carbon atom split off hydrogen fluoride much more readily than compounds which contain two or more fluorine atoms on the same carbon atom. It is thus not unexpected that polyvinyl fluoride, which consists entirely of $-CH_2{\cdot}CHF{\cdot}CH_2{\cdot}CHF-$ units,[2] should be thermally less stable than polyethylene or poly-1 : 1-difluoroethylene,[5] which contains only $-CH_2{\cdot}CF_2{\cdot}CH_2{\cdot}CF_2-$ units. The apparently anomalous position [9] of polytrifluoroethylene in the stability sequence can now be explained. This polymer is not made up of only $-CHF{\cdot}CF_2{\cdot}CHF{\cdot}CF_2-$ units arranged as $[-CHF{\cdot}CF_2{\cdot}CHF{\cdot}CF_2-]_n$ as hitherto assumed; such units would be thermally more stable than $-CH_2{\cdot}CF_2{\cdot}CH_2{\cdot}CF_2-$ units, since the hydrogen

[6] Tarrant and Lilyquist, *J. Amer. Chem. Soc.*, 1955, **77**, 3640.
[7] Tarrant, Lovelace, and Lilyquist, *ibid.*, 1955, **77**, 2783.
[8] Haszeldine, *J.*, 1955, 4291, 4302.
[9] Madorsky, Hart, Straus, and Sedlak, *J. Res. Nat. Bur. Standards*, 1953, **51**, 327.

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of a $-CF_2\cdot CHF\cdot CF_2-$ group is split off as proton or atom with less readiness than the hydrogen of a $-CF_2\cdot CH_2\cdot CF_2-$ group which tends towards the polyethylene type. The $-CHF\cdot CF_2\cdot CF_2\cdot CHF-$ units in polytrifluoroethylene, if flanked by CF_2 groups, would similarly be at least as stable as $-CH_2\cdot CF_2\cdot CH_2\cdot CF_2-$ units. It is the $-CHF\cdot CHF-$ groups in the $-CF_2\cdot CHF\cdot CHF\cdot CF_2-$ units (flanked by CF_2 or CHF groups) in polytrifluoroethylene which are the main cause of thermal instability, since hydrogen fluoride is readily eliminated to give groups such as $-CF_2\cdot CF{:}CH\cdot CF_2-$ which then break down further.

It can thus be predicted that the polymer $[-CHF\cdot CHF-]_n$ prepared from the new fluoro-olefin 1 : 2-difluoroethylene described above will show relatively poor thermal stability for a fluoro-polymer, *i.e.*, will be less stable than polyethylene.

Experimental

Preparation of Trifluoroethylene.—The olefin, prepared in 85% yield by the dehalogenation with zinc and ethanol of 1-bromo-2-chloro-1 : 1 : 2-trifluoroethane, was purified by distillation *in vacuo* (Found: *M*, 82. Calc. for C_2HF_3: *M*, 82); its purity was checked by means of its infrared spectrum.

Reaction of Trifluoroiodomethane with Trifluoroethylene.—In the dark. There was no reaction when trifluoroiodomethane (8·0 g.) and trifluoroethylene (2·4 g.) were sealed in a Pyrex tube and kept in the dark for 6 weeks.

In ultraviolet light. (a) *In Pyrex vessels.* The olefin (1·6 g., 0·02 mole) and trifluoroiodomethane (9·0 g., 0·046 mole) in a 150-ml. Pyrex tube were exposed to ultraviolet light for 3 weeks with the lower portion of the tube shielded. Distillation of the combined products from several such reactions gave, per experiment, unchanged reactants (8·6 g., 81%) and liquid products (1·9 g.), which were redistilled to give $CF_3\cdot[C_2HF_3]\cdot I$ (1·7 g., 85% based on trifluoroethylene consumed) as a 4 : 1 mixture, b. p. 62—63°, n_D^{20} 1·355, of 1 : 1 : 1 : 2 : 3 : 3-hexafluoro-3-iodopropane and 1 : 1 : 1 : 2 : 2 : 3-hexafluoro-3-iodopropane (Found: C, 12·8; H, 0·4%; *M*, 274. Calc. for C_3HIF_6: C, 12·9; H, 0·4%; *M*, 278). A small amount (*ca.* 0·1 g.) of material of higher b. p. was also isolated. The $CF_3\cdot[C_2HF_3]\cdot I$ had ultraviolet spectra: Vapour, $\lambda_{max.}$ 268 (ε 190); $\lambda_{min.}$ 227 (ε 23). In light petroleum, $\lambda_{max.}$ 268 (ε 255); $\lambda_{min.}$ 223 (ε 50).

(b) *In silica vessels with an excess of trifluoroiodomethane.* Trifluoroiodomethane (16·1 g., 0·083 mole) and trifluoroethylene (1·21 g., 0·015 mole) were exposed to ultraviolet light for 4 days in a 200-ml. silica vessel with the lower portion shielded. Distillation gave trifluoroiodomethane (13·0 g.), $CF_3\cdot(C_2HF_3)\cdot I$ (3·5 g., 85%), b. p. 62—63°, and a fraction with a higher b. p. (0·7 g.). Infrared spectroscopy showed that the $CF_3\cdot(C_2HF_3)\cdot I$ fraction had the same composition as that obtained in (a) above.

(c) *In silica vessels with an equimolar ratio.* Trifluoroiodomethane (6·5 g., 0·033 mole) and trifluoroethylene (2·5 g., 0·031 mole), treated as in (b) above, gave trifluoroiodomethane (3·5 g.) and liquid products (4·7 g.). Redistillation of the liquid products gave the 1 : 1 addition product $CF_3\cdot(C_2HF_3)\cdot I$ (3·5 g., 41%), b. p. 61—66°, shown by infrared spectroscopy to be identical with the material obtained as in (a) and (b) above, and $CF_3\cdot[C_2HF_3]_2\cdot I$ (0·8 g., 7%), b. p. 112—118° (mainly 115—116°), n_D^{20} 1·370 (Found: C, 16·1; H, 0·7. Calc. for $C_5H_2IF_9$: C, 16·7; H, 0·6%). The last material, a mixture of the compounds $CF_3\cdot CHF\cdot CF_2\cdot CHF\cdot CF_2I$ (mainly) and $CF_3\cdot CHF\cdot CF_2\cdot CF_2\cdot CHFI$, $CF_3\cdot CF_2\cdot CHF\cdot CHF\cdot CF_2I$, and $CF_3\cdot CF_2\cdot CHF\cdot CF_2\cdot CHFI$, was characterised by infrared bands at 7·20, 7·75, 8·25, 8·36, 9·00, 10·41, 11·84, and 14·50 μ. A small amount of polymer remained in the distillation flask.

Reaction of the 1 : 1 *Addition Product* $CF_3\cdot(C_2HF_3)\cdot I$ *with Chlorine.*—In a typical experiment, the adduct (1·45 g.) was sealed with chlorine (2·0 g.) and water (0·5 ml.) in a 20-ml. silica vessel and exposed to ultraviolet light for 14 days. After reaction with mercury to remove the iodine chlorides and the excess of chlorine, the volatile products were distilled *in vacuo* to give $CF_3\cdot(C_2ClF_3)\cdot Cl$ (0·99 g., 86%) (Found: *M*, 221. Calc. for $C_2Cl_2F_6$: *M*, 221). Infrared spectroscopy showed that this material was 1 : 2- (*ca.* 80%) and 1 : 1-dichlorohexafluoropropane (*ca.* 20%). The characteristic infrared bands for $CF_3\cdot CFCl\cdot CF_2Cl$ (C.S. 37) * are 7·80, 8·07, 8·84, 9·34, 9·58, 10·31, 11·75, and 13·76 μ, and for $CF_3\cdot CF_2\cdot CFCl_2$ (C.S. 36) are 7·55, 8·07, 8·25, 8·97, 11·03, 11·93, and 13·54 μ.

* See *J.*, 1955, 4500, 4501.

In a typical experiment, the mixture of dichlorides (0·99 g.), stirred with zinc dust (4 g.) and ethanol (5 ml.) in a sealed vessel at 40° for 24 hr., yielded volatile products fractionated *in vacuo* to give hexafluoropropene (0·455 g., 67%) (Found: *M*, 150. Calc. for C_3F_6: *M*, 150) and 1-chloro-1 : 2 : 2 : 3 : 3 : 3-hexafluoropropane (0·132 g., 16%) (Found: *M*, 184. Calc. for C_3HClF_6: *M*, 186·5), identified by means of their infrared spectra.[3]

The above reactions were repeated with the adduct (1·02 g.) derived from experiments in Pyrex vessels. The dichlorides (0·68 g., 85%) gave hexafluoropropene (0·34 g., 72%) and 1-chloro-1 : 2 : 2 : 3 : 3 : 3-hexafluoropropane (0·08 g., 14%).

Reaction of the toluene-*p*-sulphonate of pentafluoropropanol (4·8 g.) with potassium fluoride[2,10] (100% excess) in refluxing diethylene glycol monobutyl ether (50 ml.) for 8 hr. gave 1 : 1 : 1 : 2 : 2 : 3-hexafluoropropane (67%) (Found: *M*, 152. Calc. for $C_3H_2F_6$: *M*, 152), collected in a trap cooled by liquid oxygen then fractionated *in vacuo*. A sample (2·1 g.) prepared in this way was sealed with chlorine (20% excess) and water (2 ml.) in a 15-ml. Pyrex tube and exposed to ultraviolet radiation for 10 days, giving 1 : 1-dichlorohexafluoropropane (Found: *M*, 221) in 84% yield. Its infrared spectrum agreed with that reported earlier.[3]

Reaction of the 1 : 1 *Addition Product* $CF_3{\cdot}(C_2HF_3){\cdot}I$ *with Bromine.*—The adduct (2·0 g.) was sealed in a Pyrex tube with bromine (1·6 g.) and exposed to ultraviolet light for 8 days to give a mixture (1·58 g., 92%) of 1-bromo-1 : 1 : 2 : 3 : 3 : 3- and 1-bromo-1 : 2 : 2 : 3 : 3 : 3-hexafluoropropane, b. p. 35° (Found: *M*, 232. Calc. for C_3HBrF_6: *M*, 231). Comparison of the infrared spectra of this material and of pure 1-bromo-1 : 1 : 2 : 3 : 3 : 3-hexafluoropropane [4] revealed the extra bands at 7·45, 9·09, 9·60, 13·3, and 14·1 μ caused by the 1-bromo-1 : 2 : 2 : 3 : 3 : 3-hexafluoropropane.

Exposure of 1 : 1 : 1 : 2 : 2 : 3-hexafluoropropane (2·6 g.), bromine (60% of theory for complete bromination), and water (1 ml.), in a 10-ml. silica tube, to ultraviolet light for 9 days gave 1-*bromo*-1 : 2 : 2 : 3 : 3 : 3-*hexafluoropropane* (76%) (Found: C, 15·6; H, 0·5%; *M*, 231. C_3HBrF_6 requires C, 15·6; H, 0·4%; *M*, 231), b. p. 35°.

Reaction of Trifluoroethylene with Hydrogen Bromide.—(a) *In the dark.* There was no reaction when trifluoroethylene (0·55 g.) and hydrogen bromide (0·55 g.) were kept in the dark in a Pyrex tube for 14 days.

(b) *Thermal.* The reaction mixture of (a) was heated at 100° for 2 days in the dark without reaction. Reaction occurred only at 200° and after 5 days gave unchanged reactants and a 50% yield of a mixture of 1-bromo-1 : 2 : 2- and 1-bromo-1 : 1 : 2-trifluoroethane.

No reaction was detected when hydrogen bromide (0·50 g.), trifluoroethylene (0·50 g.), and glacial acetic acid (4 ml.) were kept in the dark for 2 days.

(c) *Photochemical.* In a typical small-scale experiment, trifluoroethylene (1·58 g., 0·019 mole) and hydrogen bromide (1·56 g., 0·019 mole) were sealed in a silica tube and exposed to light. An immediate reaction was apparent and after 30 min. distillation gave a mixture (3·07 g., 98%) (vapour-pressure 760 mm. at 34°) of 1-bromo-1 : 2 : 2- and 1-bromo-1 : 1 : 2-trifluoroethane (Found: C, 15·0; H, 1·9%; *M*, 164. Calc. for $C_2H_2BrF_3$: C, 14·7; H, 1·2%; *M*, 165). Henne and Renoll [11] report b. p. 40—41°/735 mm. for 1-bromo-1 : 2 : 2-trifluoroethane, and Swarts [12] reports b. p. 25° for 1-bromo-1 : 1 : 2-trifluoroethane.

An experiment on a larger scale with trifluoroethylene (8·05 g.) and hydrogen bromide (8·02 g.), irradiated for 1 hr., gave a mixture (15·8 g., 98%) of the bromo-compounds. This was separated by distillation into 1-bromo-1 : 1 : 2- (38%) and 1-bromo-1 : 2 : 2-trifluoroethane (53%) with an intermediate fraction which spectroscopic examination showed to have essentially the same composition as the original mixture. If the intermediate fraction is assumed to contain 53% of $CHFBr{\cdot}CHF_2$ and 38% of $CF_2Br{\cdot}CH_2F$, the photochemical reaction of hydrogen bromide with trifluoroethylene has thus produced 57% of $CHFBr{\cdot}CHF_2$ and 43% of $CF_2Br{\cdot}CH_2F$. These figures agree well with the analysis based on zinc and ethanol treatment (see below) used for experiments carried out on a smaller scale.

Reaction of the 1 : 1 *Addition Product* $C_2H_2F_3Br$ *with Zinc and Ethanol.*—The adduct (3·39 g.) was sealed in a Pyrex tube with zinc dust (10 g.) and ethanol (5 ml.) and heated in a rotating furnace at 85° for 24 hr. The volatile products were washed with water and distilled repeatedly *in vacuo* through traps cooled to −95°, −140°, and −183°. The fraction which condensed at

[10] Tiers, Brown, and Reid, *J. Amer. Chem. Soc.*, 1953, **75**, 5978; Edgell and Parts, *ibid.*, 1955, 77, 4899.
[11] Henne and Renoll, *ibid.*, 1936, **58**, 887.
[12] Swarts, *Bull. Acad. roy. Belg.*, 1911, 563.

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−140° was (cis + trans)-1 : 2-*difluoroethylene* (0·683 g., 51%), b. p. −28° (isoteniscope) (Found : F, 58·8%; *M*, 64. $C_2H_2F_2$ requires F, 59·3%; *M*, 64), shown to be free from 1 : 1-difluoroethylene by infrared spectroscopy. Spectroscopic examination of the fraction which condensed at −183° (0·600 g., 45%) showed that it was 1 : 1-difluoroethylene contaminated with a small amount of one of the isomers of 1 : 2-difluoroethylene (Found : *M*, 64. Calc. for $C_2H_2F_2$: *M*, 64). The mixture was therefore sealed with chlorine (0·66 g.) and allowed to warm from −80° to 20° during 12 hr., then exposed to light for 2 hr. Distillation gave the mixed dichlorides (1·23 g., 98%) shown by infrared spectroscopy to contain 1 : 2-dichloro-1 : 1-difluoroethane (*ca.* 90%) and 1 : 2-dichloro-1 : 2-difluoroethane (10%).

1 : 2-Difluoroethylene (0·65 g.), prepared as above, was sealed with chlorine (0·72 g.) and, to prevent an explosive reaction, was allowed to warm from −80° to room temperature during 12 hr. The reaction was completed by exposure to ultraviolet light for 1 hr. Distillation gave 1 : 2-dichloro-1 : 2-difluoroethane (1·36 g., 99%), b. p. 58°, n_D^{20} 1·376. Henne and Waalkes [13] report b. p. 59°, n_D^{20} 1·391.

A known specimen of 1 : 2-dichloro-1 : 1-difluoroethane was prepared by reaction of 1 : 1-difluoroethylene (1·2 g.) and chlorine (1·04 g.) in the dark for 12 hr. followed by exposure to ultraviolet light for 2 hr. The product (1·96 g., 98%) had b. p. 47°. Henne and Hubbard [14] report b. p. 46·8°, n_D^{20} 1·3619.

The above experiments show that the mixture of difluoroethylenes obtained from the reaction of the addition product $C_2H_2F_3Br$ with zinc and ethanol contained 56% of 1 : 2-difluoroethylene and 41% of 1 : 1-difluoroethylene, *i.e.*, CHF:CHF to CF_2:CH_2 = 1·36 to 1, and $CHFBr{\cdot}CHF_2$ to $CF_2Br{\cdot}CH_2F$ = 58 to 42.

1 : 2-Difluoroethylene shows infrared bands at 3·19 (C–H), 5·76, 5·83 (strong doublet, C:C stretch.), 6·25, 6·33 (weak doublet), 7·22, 7·26, 7·33 (triplet), 7·86, 7·97, 8·78, 8·85, 8·95 (triplet), 9·77, 10·00, 12·83, 13·00, 13·23 μ (triplet).

Reaction of the 1 : 1 *Addition Product* $C_2H_2F_3Br$ *with Mercurous Fluoride.*—The adduct (1·65 g.) was sealed in a Pyrex tube with mercurous fluoride (5 g.) and heated at 120—140° for 2 days. Distillation gave unchanged starting material (1·26 g., 77%) and a mixture of 1 : 1 : 1 : 2- and 1 : 1 : 2 : 2-tetrafluoroethane (0·163 g., 70%), b. p. −24° (Found : *M*, 101·5. Calc. for $C_2H_2F_4$: *M*, 102). The infrared spectrum of the recovered bromo-compounds was slightly different from that of the starting material, *i.e.*, preferential replacement of bromine by fluorine in one isomer was occurring to a limited extent.

Reaction of Trifluoroethylene with Hydrogen Chloride.—The olefin (1·35 g., 0·0165 mole) and anhydrous hydrogen chloride (0·61 g., 0·0167 mole), heated to 200° for 2 days, showed no reaction, but after 2 days at 240° gave 1-*chloro*-1 : 1 : 2-*trifluoroethane* (0·64 g., 33% conversion), b. p. 12° (Found : C, 20·6; H, 2·1%; *M*, 119. $C_2H_2ClF_3$ requires C, 20·3; H, 1·7%; *M*, 118·5). Swarts [15] reports b. p. 17° for the isomer 1-chloro-1 : 2 : 2-trifluoroethane.

The structure of the product from hydrogen chloride and trifluoroethylene was shown by treatment of a sample (0·53 g.) with zinc dust (3 g.) and ethanol (5 ml.) in a sealed Pyrex tube at 80—90° for 8 hr. Only 1 : 1-difluoroethylene (85% yield), shown by spectroscopic examination to be uncontaminated by 1 : 2-difluoroethylene, 1 : 2 : 2-trifluoroethane, or vinyl fluoride, was produced.

Reaction of Trifluoroethylene with Iodine Monochloride.—The olefin (1·33 g., 0·016 mole) and iodine monochloride (2·05 g., 0·013 mole), set aside for 12 hr., gave unchanged olefin (0·33 g.) and 1-*chloro*-1 : 1 : 2-*trifluoro*-2-*iodoethane* (2·95 g., 97%), b. p. 82—83°, n_D^{20} 1·433 (Found : C, 9·7; H, 0·7. C_2HClIF_3 requires C, 9·8; H, 0·4%). Ultraviolet spectrum in light petroleum : $\lambda_{max.}$ 265 (ε 295); $\lambda_{min.}$ 218 (ε 45); cf. $CF_2I{\cdot}CHFCl$ in light petroleum : $\lambda_{max.}$ 269 (ε 290), $\lambda_{min.}$ 223 (ε 40).

One of us (B. R. S.) is indebted to the Department of Scientific and Industrial Research for a Maintenance Allowance, 1950—1953.

University Chemical Laboratory, Cambridge. [*Received, February 5th,* 1957.]

[13] Henne and Waalkes, *J. Amer. Chem. Soc.*, 1945, **67**, 1639.
[14] Henne and Hubbard, *ibid.*, 1936, **58**, 404.
[15] Swarts, Mémoires couronnés et autre Mémoires publiés par l'Academie royale de Belgique, 1901, 61; *Zent.*, 1903, I, 13.

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541. *The Photodecomposition of Acetaldehyde Catalysed by Thiols.*

By R. N. Birrell, R. F. Smith, A. F. Trotman-Dickenson, and H. Wilkie.

The photo-initiated thermal decomposition of acetaldehyde catalysed by alkanethiols and hydrogen sulphide has been investigated between 168° and 396°. The catalytic effect of the thiols is independent of their concentration over a limited range and is a function of the structure of the thiol so that the relative effects are: $H_2S > MeSH > EtSH > Pr^iSH > Bu^tSH$.

It is established that thiols react readily with free radicals. This finds application in the use of thiols as chain-transfer agents in free-radical polymerisation. However, very few kinetic studies of reactions involving thiols and RS· radicals have been reported. The only comprehensive study of thiol-catalysis appears to be that of Barrett and Waters,[1] on the catalysis of the decarbonylation of several saturated aliphatic aldehydes by alkanethiols in the liquid phase. The reaction chains were initiated by the thermal decomposition of dimethyl αα′-azo*iso*butyrate and αα′-azo*iso*butyronitrile. They supposed that the catalysis could be attributed to the supersession of the reaction (1′)

$$R\cdot + R{\cdot}CHO = RH + R\cdot + CO \quad (1')$$

by the faster cycle (2′, 3′)

$$R\cdot + R'SH = RH + R'S\cdot \quad (2')$$

$$R'S\cdot + R{\cdot}CHO = R'SH + R\cdot + CO \quad (3')$$

The predominant chain-carrying step in the high-temperature photo-initiated decomposition of acetaldehyde in the vapour phase is almost certainly (1):[2]

$$Me\cdot + Me{\cdot}CHO = CH_4 + Me\cdot + CO \quad (1)$$

It appeared of interest to study the effect of adding thiols to the system, to see if reaction (1) would be superseded by the reactions equivalent to (2′) and (3′). Experiments were therefore carried out with a number of thiols over a range of temperature. It was hoped that information would be obtained on the effect of structure on the reactivity of the thiols and on the relative rate constants of the reactions.

Experimental

Materials.—Acetaldehyde was prepared by distillation of paraldehyde containing a little sulphuric acid; it was thoroughly degassed before use, and stored as a gas in a blackened bulb. The hydrogen sulphide was generated in a Kipp's apparatus, dried, and degassed before use. The thiols were commerial samples; they were thoroughly degassed.

Apparatus.—The reactions were carried out in two very similar Pyrex reaction vessels, of about 200 c.c. each, placed side by side in an electric furnace with a quartz window. They were illuminated by the full light from a medium-pressure mercury arc which was allowed to warm for at least 20 min. before a run. The lamp was run continuously throughout a series of runs. Some runs with methanethiol were carried out with twin quartz cells. One of the cells was connected to a mercury manometer: the other to a di-*n*-butyl phthalate manometer for the measurement of the small quantities of thiol and to a Bourdon gauge with an optical lever for the measurement of the total pressure. When the cells were filled to the same pressure of pure acetaldehyde, the difference in the rates of photolysis was not significant. The cells, manometers, and storage bulbs were attached to a conventional vacuum-line.

Procedure.—A convenient pressure of thiol was admitted to one of the cells. Identical partial pressures of acetaldehyde were then admitted to both cells. The dead space was small, so that the measured pressures of reactants corresponded closely to the composition of the mixtures in the cells. After a few minutes (to allow the gases to come to the required temperature), light was admitted to the cells. The change in total pressure in each was then followed

[1] Barrett and Waters, *Discuss. Faraday Soc.*, 1953, **14**, 221.
[2] Steacie, "Atomic and Free Radical Reactions," Reinhold Publ. Corp., New York, 2nd edn., 1954.

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on a manometer. Measurements of the total pressures were made at conveniently spaced intervals.

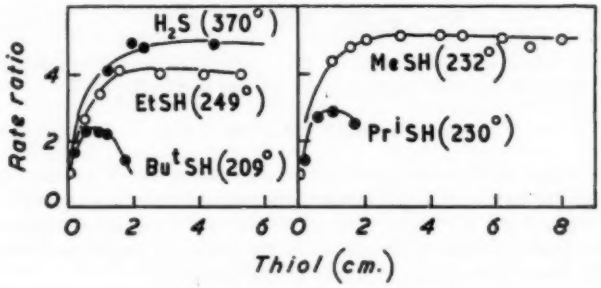
Results and Discussion

It has been established by many workers that the products of the photo-initiated thermal decomposition of acetaldehyde are almost exclusively methane and carbon monoxide. In confirmation we found that the pressure in the vessel containing pure acetaldehyde approximately doubled when the run was carried to completion. The ultimate pressure increase in the vessel containing the thiol was always about 10% less than the initial partial pressure of acetaldehyde.

The catalytic effect of the thiol was determined from observations taken at the beginning of the reaction. The time taken for an increase in pressure equal to one-fifth of the initial pressure of acetaldehyde was measured for the catalysed and the uncatalysed system. It was found that substantially the same ratio was obtained if the initial slopes of the decomposition curves were measured or the ratios of the times taken to reach some other small degree of decomposition.

Most work was carried out with methanethiol as the catalyst. It was found that at a given temperature and pressure of acetaldehyde the catalytic effect of the thiol increased

Fig. 1. *Typical variations of catalytic effect with concentration.*



as its concentration was increased. Then the effect remained constant over a considerable range of concentration. Finally, when the thiol concentration was about three-quarters of the acetaldehyde concentration, the ratio increased at low light intensities. The variation of the ratio with concentration is shown in Fig. 1. All the points shown were obtained with an initial pressure of 10 cm. of acetaldehyde and with the same incident light intensity. It was found that in the concentration range represented by the flat portion of the curve no alteration in the ratio was brought about by doubling the aldehyde concentration or by varying the incident light intensity by a factor of four. The values of the constant rate ratios were determined at five temperatures between 189° and 396°. The values obtained have been plotted on the Arrhenius plot, Fig. 2.

Similar results were obtained from the experiments in quartz reaction vessels, though the rate ratios were always somewhat higher. It is likely that some reaction chains were initiated by the photolysis of the thiol by the unfiltered light from the mercury arc.

Similar experiments were carried out with each of the other thiols. Again it was found that for hydrogen sulphide and ethanethiol, the rate ratio increased with increasing thiol concentration until it reached a constant value (Fig. 1). With ethanethiol as catalyst the rate ratios were independent of a variation in absorbed light intensity by a factor of nine. The interpretation of the results with hydrogen sulphide is more uncertain. A slight induction period was evident at low light intensities and high concentrations of the sulphide. The rate ratios corresponding to the plateau are plotted against temperature for both catalysts in Fig. 2.

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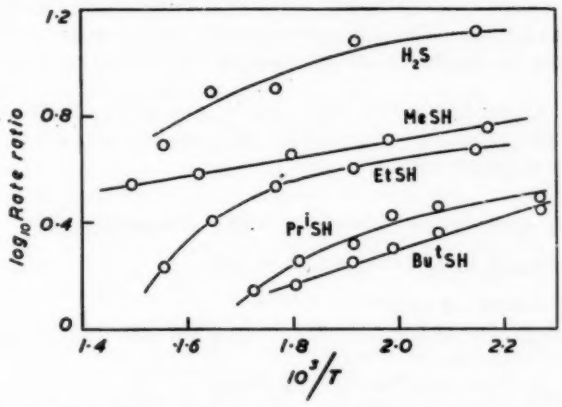
The catalytic behaviour of propane-2-thiol and 2-methylpropane-2-thiol is shown in Fig. 1. A constant rate ratio is never maintained over any considerable range of concentration, though the rate ratios are independent of a variation of light intensity by a factor of four. For purposes of comparison the maximum rate ratios for these catalysts are plotted against temperature in Fig. 2. At temperatures above 300° a small quantity of 2-methylpropane-2-thiol reduced the rate of the decomposition of acetaldehyde to negligible proportions. Propane-2-thiol behaved in the same manner at temperatures about 40° higher. There was no evidence that this inhibition was caused by products of the thermal decomposition of the thiols.

FIG. 2. *Arrhenius plot for the catalytic effect of the thiols.*



The mechanism of the photo-initiated thermal decomposition of acetaldehyde has often been written [2] as :

$$\left.\begin{aligned} \mathrm{Me{\cdot}CHO} + h\nu &= \mathrm{Me{\cdot}} + \mathrm{H{\cdot}CO{\cdot}} \\ \mathrm{H{\cdot}CO{\cdot}} &= \mathrm{H{\cdot}} + \mathrm{CO} \\ \mathrm{H{\cdot}} + \mathrm{Me{\cdot}CHO} &= \mathrm{H_2} + \mathrm{Me{\cdot}} + \mathrm{CO} \end{aligned}\right\} I_{abs.}$$

$$\mathrm{Me{\cdot}} + \mathrm{Me{\cdot}CHO} = \mathrm{CH_4} + \mathrm{Me{\cdot}} + \mathrm{CO} \quad \ldots\ldots\ldots (1)$$

$$2\mathrm{Me{\cdot}} = \mathrm{C_2H_6} \quad \ldots\ldots\ldots\ldots (4)$$

It is now known that this is not a complete description, but it certainly represents the principal reactions correctly. A mechanism similar to that proposed by Barrett and Waters is adequate to cover the facts of the catalysis by methanethiol. The steps immediately consequent upon the absorption of light are followed by :

$$\mathrm{Me{\cdot}} + \mathrm{Me{\cdot}SH} = \mathrm{CH_4} + \mathrm{MeS{\cdot}} \quad \ldots\ldots\ldots (2)$$

$$\mathrm{MeS{\cdot}} + \mathrm{Me{\cdot}CHO} = \mathrm{MeSH} + \mathrm{Me{\cdot}} + \mathrm{CO} \quad \ldots\ldots\ldots (3)$$

$$2\mathrm{MeS{\cdot}} = \mathrm{Me_2S_2} \quad \ldots\ldots\ldots\ldots (5)$$

Disulphides have been found [1] in the products of thiol-catalysed reactions at low temperatures, which supports the postulation of reaction 5.

The observed kinetics can only be simply explained on the assumption that the combination of RS· radicals is the chain-ending reaction. This reaction is very unlikely to have a greater rate constant than that for the combination of methyl radicals or the reaction of an RS· radical with a methyl radical. Consequently the steady-state concentration of RS· radicals must be much greater than that of methyl. This will only be so if k_2, the rate constant for reaction (2), is very much greater than k_1 or k_3. Unpublished results of Mr. J. A. Kerr in this Laboratory indicate that at low temperatures k_2 is at least fifty times k_1.

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Solution of the steady-state equations yields (when the decomposition in the initiating step is neglected) :

$$-\mathrm{d[Me{\cdot}CHO]}/\mathrm{d}t = k_1(I_0/k_4)^{\frac{1}{2}}[\mathrm{Me{\cdot}CHO}]$$

for the uncatalysed reaction, and :

$$-\mathrm{d[Me{\cdot}CHO]}/\mathrm{d}t = k_3(I_0/k_5)^{\frac{1}{2}}[\mathrm{Me{\cdot}CHO}]$$

for the catalysed reaction.

$$\text{Rate ratio} = \frac{k_3(I_0/k_5)^{\frac{1}{2}}[\mathrm{Me{\cdot}CHO}]}{k_1(I_0/k_4)^{\frac{1}{2}}[\mathrm{Me{\cdot}CHO}]} = \frac{k_3k_4^{\frac{1}{2}}}{k_1k_5^{\frac{1}{2}}}$$

This equation should apply to the rate ratios in the region where they are independent of the thiol concentration. The rate ratio probably increases initially with thiol concentration because, at the lowest ratios, reaction (2) is not sufficiently faster than reaction (1).

Since k_1 and k_4 are known,[3,4] $k_3/k_5^{\frac{1}{2}}$ can be evaluated. From the temperature coefficient of the rate ratio, $E_3 - E_1 - \frac{1}{2}E_5 + \frac{1}{2}E_4$ can be found where the E's are the activation energies of the reactions.

Hence, assuming

$$\log_{10} k_1 \text{ (mole}^{-1} \text{ cm.}^3 \text{ sec.}^{-1}) = 12{\cdot}1 - (8400/2{\cdot}303\boldsymbol{R}T)$$
$$\log_{10} k_4 \text{ (mole}^{-1} \text{ cm.}^3 \text{ sec.}^{-1}) = 13{\cdot}3$$

we find $E_3 - \frac{1}{2}E_5 = 6800$ cal. mole^{-1}.

Most combinations of small free radicals have very low activation energies and A factors of about $10^{13{\cdot}3}$ mole^{-1} cm.^{3} sec.$^{-1}$.

Assuming $\log_{10} k_5$ (mole^{-1} cm.^{3} sec.$^{-1}$) $= 13{\cdot}3$ gives :

$$\log_{10} k_3 \text{ (mole}^{-1} \text{ cm.}^3 \text{ sec.}^{-1}) = 11{\cdot}9 - (6800/2{\cdot}303\boldsymbol{R}T)$$

This value of k_3 is probably reliable. The only cause for doubt is that the same simple mechanism will not describe the behaviour of the other thiols. However, the rate ratios with each of the catalysts were independent of their concentration over a detectable range, and also of the absorbed light intensity. These facts can only be readily interpreted on the assumption that reaction (2′) represents the fate of virtually all the alkyl radicals released into the system. Therefore it seems probable that a mechanism substantially parallel to that for methanethiol holds for the other compounds, but that other side reactions must occur. In these circumstances it is impossible to derive rate constants for the elementary reactions. The rate ratio was found to reach its constant value for a lower concentration of methanethiol than for hydrogen sulphide. From such evidence the apparent order of reactivity for methyl radicals with the thiols (reaction 2′) may be deduced :

$$\mathrm{Bu^tSH} > \mathrm{Pr^iSH} > \mathrm{EtSH} > \mathrm{MeSH} > \mathrm{H_2S}$$

This order is the opposite to that for the catalytic effect of the thiols ($k_3/k_5^{\frac{1}{2}}$). This is understandable : the first reaction would presumably be favoured by a weakening of the S–H bond, whereas the second would be favoured by its strengthening.

We are indebted to the British Petroleum Company for a grant in aid of this work.

Department of Chemistry,
The University, Edinburgh.

[*Received, February 12th,* 1957.]

[3] Dodd, *Canad. J. Chem.*, 1955, **33**, 699.
[4] Shepp, *J. Chem. Phys.*, 1956, **24**, 939.

542. *The Decomposition of Nitramide in Anisole Catalysed by Aniline Derivatives.*

By G. C. Fettes, J. A. Kerr, A. McClure, J. S. Slater, C. Steel, and A. F. Trotman-Dickenson.

Decomposition of nitramide catalysed by primary, secondary, and tertiary aniline derivatives in anisole has been investigated between 7° and 55°. Activation energies for the catalytic coefficients have been determined. The catalytic coefficients at 25° are related to the activation energies by the expression

$$\log_{10} k_c\ (25°)\ (\text{mole}^{-1}\ \text{kg. min.}^{-1}) = 23{\cdot}2 - 1{\cdot}63E\ (\text{kcal. mole}^{-1})$$

The catalytic coefficients of a series of acidic or basic catalysts for a reaction are normally related to their respective dissociation constants by the Brönsted relation. In theoretical discussions of this kind of free-energy relation it is generally supposed that the difference in the catalytic power of the various catalysts can be attributed to the different activation energies of the fundamental protolytic reactions.[1] The temperature coefficients of comparatively few reactions catalysed by acids or bases have been measured. Consequently it is difficult to say whether there is any real basis for the supposition. Further, most of the reactions for which temperature coefficients have been measured have been studied in aqueous solution. It is known that ionic processes in aqueous solution frequently do not conform to the simplest types of energy relation. Accordingly it is not surprising that the results obtained with aqueous solutions do not often yield simple relations between the catalytic coefficients and activation energies.

This work was undertaken to obtain results in a solvent which does not readily form hydrogen bonds. The decomposition of nitramide was chosen because it has been very fully investigated and can easily be followed.[1] Anisole is a convenient solvent which can easily be sufficiently purified and in which a considerable amount of work has been done. Substituted anilines were chosen as catalysts because they have also been fairly fully studied.[1-4]

Experimental

Materials.—Anisole was dried ($CaCl_2$) and fractionated on an 18″ column packed with glass helices. Several batches were purified; all behaved similarly. Aniline derivatives were distilled over potassium hydroxide pellets under reduced pressure and stored in sealed containers. Nitramide was prepared by the method of Marlies, LaMer, and Greenspan [5] and stored in a refrigerator as a solution in anisole.

Apparatus and Procedure.—The runs were carried out in reaction vessels similar to those used by Bell and Caldin.[3] The faster runs were carried out in vessels with taps, the slower runs in sealed vessels. The vessels were placed in a glass-fronted thermostat maintained to ±0·02° and were agitated by percussion. Reaction mixtures were made up by weight. First, a convenient quantity of catalyst (or catalyst solution for the stronger bases) was weighed in a weighing bottle. Anisole, to make approximately 2 g. of mixture, was then added. Finally, 2 c.c. of nitramide solution were added immediately before the mixture was introduced into the reaction vessel.

The runs were followed by observing the increase in pressure of the evolved gas. First-order plots were then drawn, based on the pressure of gas after complete reaction. In the slowest runs the reaction vessels were placed in a warm bath to bring the reaction to completion overnight. The rate constants were deduced from the observations taken during the first two half-lives of the reactions, after which some of the plots tailed off. The catalytic coefficients

[1] Bell, " Acid–Base Catalysis," Oxford, 1941.
[2] Bell and Caldin, *Trans. Faraday Soc.*, 1951, **47**, 50; Caldin and Peacock, *ibid.*, 1955, **51**, 1217.
[3] Bell and Trotman-Dickenson, *J.*, 1949, 1288.
[4] Bell and Wilson, *Trans. Faraday Soc.*, 1950, **46**, 407.
[5] Marlies, LaMer, and Greenspan, *Inorg. Synth.*, 1939, **1**, 68.

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of the bases were found to be a function of the concentration of the solutions. The extrapolations devised by Bell and Trotman-Dickenson [3] were used to obtain the true coefficients.

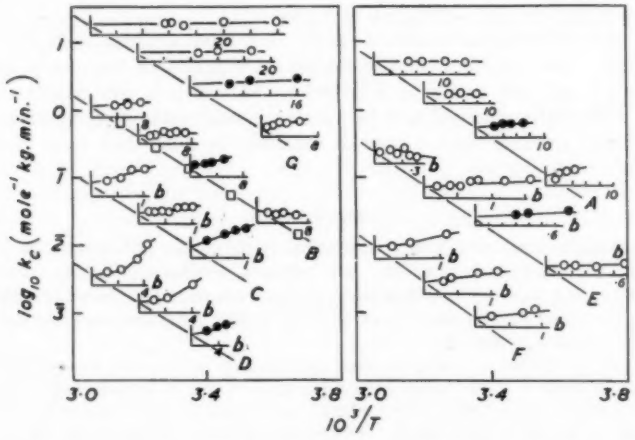
Results

The results of the kinetic measurements are included in Arrhenius plots (Fig. 1*a* and *b*) which show the catalytic coefficients from the individual runs and the extrapolations employed.

Base	Catalytic coefficients, $10^3 k_c$ (mole^{-1} kg. min.$^{-1}$) (temp. in parentheses)				$\log_{10} A$	E (kcal. mole^{-1})
Diethyl-*p*-toluidine ...	480 (7·6°)	2295 (25·0°)	6760 (39·6°)	17,340 (54·1)°	9·43	13·9
Dimethyl-*p*-toluidine	105 (7·6)	599 (25·0)	1730 (39·6)	4875 (54·1)	9·22	14·5
Dimethylaniline	31 (8·6)	150 (25·0)	425 (40·0)	1230 (54·1)	8·81	14·8
Methylaniline	4·28 (7·7)	27·6 (25·0)	72·3 (40·0)	242 (54·1)	8·17	15·0
Aniline	—	8·07 (25·0)	30·0 (40·0)	80·0 (54·0	8·21	15·5
m-Chloroaniline	—	0·85 (25·0)	2·90 (39·6)	9·5 (54·1)	7·44	16·1
o-Chloroaniline	—	0·20 (25·0)	1·43 (40·0)	3·80 (54·1)	5·87	14·1

The results are summarized in the Table. Generally they agree very well with those of Bell and Trotman-Dickenson [3] and Bell and Caldin,[2] those for *m*-chloroaniline being the only exceptions (we can suggest no reason for the discrepancy; the identity of the present material

FIG. 1*a and b*. *Arrhenius plots for the decomposition of nitramide in anisole catalysed by aniline derivatives. The individual points and the extrapolations are shown.* ○, *This work*; ●, *Bell and Trotman-Dickenson* [3]; □, *Bell and Caldin.*[2] *Concentrations are in moles kg.*$^{-1}$. *Except where the scale is marked b when the second method of extrapolation was used, the concentration scale on the abscissæ is for* $1/\sqrt{b}$ *corresponding to the first method of extrapolation. A, Dimethyl-*p*-toluidine; B, dimethylaniline; C, aniline; D, o-chloroaniline; E, methylaniline; F,* m*-chloroaniline; G, diethyl-*p*-toluidine.*



was confirmed by measurement of its refractive index and of the m. p. of its benzoyl derivative). The accuracy of the determination of the activation energies cannot be readily assessed because of the need for the extrapolation. An error of $\pm 0{\cdot}3$ kcal. mole^{-1} may reasonably be assigned.

Discussion

The activation energies of the catalytic coefficients are plotted against the catalytic coefficients of the various bases at 25° in Fig. 2. All except that for *o*-chloroaniline lie on a straight line given by $\log_{10} k_c\,(25°) = 23{\cdot}2 - 1{\cdot}63E$. The deviation of the *ortho*-substituted compound is not surprising; many free-energy relations break down for *ortho*-compounds. The slope of the line in Fig. 2 differs markedly from that which would be obtained (broken line) if all the differences between the catalytic coefficients could be attributed to variations in activation energy. The line representing the variation of $\log_{10} k_c$ with E deviates from

the " theoretical " slope, which corresponds to a constant value of A, for many series of reactions. Usually the slope is too great, *i.e.*, systematic changes in A compensate for the variations in E. In the present reaction the reverse occurs; A is not constant; it varies so as to reinforce the changes in E.

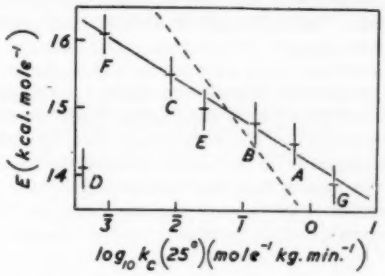


FIG. 2. *Relation between activation energies and catalytic coefficients for the aniline-catalysed decomposition of nitramide. A—G, see Fig.* 1. *Slope of broken line* $= 2{\cdot}303RT$.

The fact that the activation energies of the primary, secondary, and tertiary bases (except *o*-chloroaniline) obey the same relation supports the interpretation of the basic strength of amines, as measured in aqueous solutions, which has been suggested by Bell and Trotman-Dickenson.[3,6]

THE UNIVERSITY, EDINBURGH, 9. [*Received, February 12th*, 1957.]

[6] Trotman-Dickenson, *J.*, 1949, 1293.

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543. *The Pyrolysis of* tert.-*Butyl Formate.*

By E. GORDON, S. J. W. PRICE, and A. F. TROTMAN-DICKENSON.

The thermal decomposition of *tert.*-butyl formate into *iso*butene and formic acid has been studied in a static system at temperatures between 230° and 300° c. The decomposition is homogeneous and obeys first-order kinetics in its early stages; the rate constant is given by

$$\log_{10} k(\text{sec.}^{-1}) = 11{\cdot}1 - (34{,}600/2{\cdot}303RT)$$

The elimination of formic acid is probably a molecular process, as the addition of *cyclo*hexene has a very small effect on the rate. The rate of this reaction is reasonably related to the rates of similar decompositions.

DETERMINATIONS of the rate constants of the decompositions of ethyl, *iso*propyl, and *tert.*-butyl chlorides, bromides, and acetates have all been reported in the literature.[1] No measurements have been reported on the decompositions of *tert.*-butyl formate although the ethyl and *iso*propyl derivatives have been investigated. The object of the present study was to fill this gap.

EXPERIMENTAL

Materials.—The *tert.*-butyl formate was specially prepared for use in this investigation by Dr. C. Barkenbus (University of Kentucky) according to his method.[2] The material was thoroughly degassed and stored in solid carbon dioxide. It was found that at temperatures appreciably above room temperature and in the absence of a drying agent the liquid rapidly decomposed, apparently into *iso*butene and formic acid. The *cyclo*hexene, which was also degassed, was freed from peroxides by shaking it with acidic ferrous sulphate solution.

[1] For full references see Trotman-Dickenson, " Gas Kinetics," Butterworths, London, 1955, and Maccoll and Thomas, *Nature*, 1955, **176**, 392.
[2] Barkenbus, Naff and Rapp, *J. Org. Chem.*, 1954, **19**, 1916.

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Apparatus.—The decomposition was studied in a 385-c.c. Pyrex bulb attached to a conventional vacuum system by heated tubing; the total dead space was approximately 13 c.c. The empty bulb had a surface : volume ratio of 0·9 cm.$^{-1}$; when it was packed with fire-polished Pyrex tubing the ratio was 3·0 cm.$^{-1}$. The bulb was contained in a mercury-vapour jacket, whose temperature could be controlled readily by varying the pressure under which the mercury boiled. The temperature of the jacket was determined by reference to standard tables of the vapour pressure of mercury. The reaction was studied by following the change in pressure in the reaction vessel on a mercury manometer.

Procedure.—Runs were started by admitting a suitable quantity of the formate to the reaction vessel from the storage bulb; in some runs *cyclo*hexene was also added. Readings of the pressure in the vessel were then recorded at convenient intervals. Rate constants were determined from first-order plots of the logarithms of the pressure changes against time, based on the assumption that complete reaction corresponded to a doubling of the pressure. The logarithmic plots were strictly linear for the first 70—80% of the reaction at the higher temperatures but thereafter tended to curve slightly. No induction periods were observed.

Results and Discussion

tert.-Butyl formate was presumed to yield formic acid and *iso*butene as the primary products of the decomposition. This presumption is based upon the known ease with which these products are formed in the liquid in the presence of a trace of acid and upon the analogy with the decompositions of the other formates. It was difficult to check this by analysis, because of the rapidity with which the liquid decomposed. Several experiments were done with a trap system in which the formate and formic acid were condensed in a trap cooled in solid carbon dioxide and the *iso*butene in a trap cooled in liquid oxygen. The *iso*butene was then transferred back into the reaction system and its pressure measured. The percentage decomposition based on the formation of *iso*butene was then calculated. The results of a series of runs at 251° were :

Percentage decomposition by pressure rise	11·4	19·0	30·0	41·0
Percentage decomposition by *iso*butene	7·9	14·4	30·0	39·0

The method of analysis was not very satisfactory, but there appears to be little doubt as to the nature of the decomposition. Runs which were followed for many half-lives never yielded a pressure greater than twice the initial pressure. This is evidence that the formic acid does not decompose at these low temperatures.

The linearity of the logarithmic plots demonstrated the first-order nature of the decomposition which was confirmed by runs with different initial pressures of the formate between 3·8 and 10·3 cm. No systematic trend or variation of the rate constants outside the limit of experimental error was observed.

Fig. 1 is an Arrhenius plot of the rate constants for the thermal decomposition. The best straight line was calculated by the method of least squares giving equal weight to each run : the points shown in the Figure are the mean values obtained at each temperature. The results are best expressed by

$$\log_{10} k(\text{sec.}^{-1}) = 11{\cdot}1 - [(34{,}600 \pm 900)/2{\cdot}303RT]$$

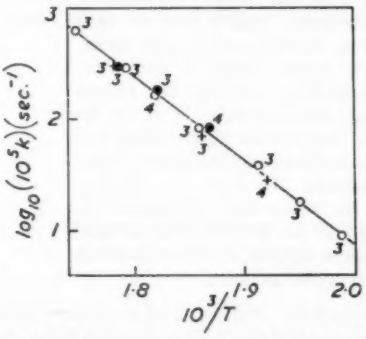
Two facts showed the decomposition to be homogeneous. First, no conditioning of the reaction vessel was needed before reproducible results were obtained. Second, packing the reaction vessel did not affect the rate constants, as is shown in Fig. 1 where the mean results obtained in the packed vessel are plotted.

The absence of an induction period and the negligible effect of packing the vessel indicate that the decomposition is molecular and does not involve free radicals. This was confirmed by adding *cyclo*hexene to the system; 20—50% of *cyclo*hexene appeared to

reduce the rate of decomposition very slightly, but the lowering was of the same order as the experimental scatter. The results obtained with *cyclo*hexene are also shown in Fig. 1.

The activation energy of this decomposition is markedly lower than those for the decomposition [3] of ethyl (44·1 kcal. mole^{-1}) and of *iso*propyl formate (44·0 kcal. mole^{-1}). However, it is often more enlightening to compare the variation of the rate constants of a

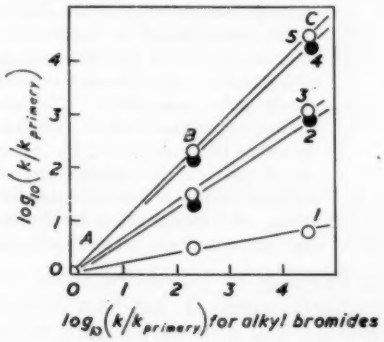
FIG. 1. *Arrhenius plot for the thermal decomposition of* tert.-*butyl formate.*



○ Unpacked vessel. ● Packed vessel. + Unpacked vessel with the addition of *cyclo*hexene.

The figures by the circles indicate the number of runs averaged to obtain each point.

FIG. 2. *The relation between the rates of the molecular decompositions of various ethyl, iso*propyl, *and* tert.-*butyl derivatives.*



A, Ethyl. *B*, *iso*Propyl. *C*, *tert.*-Butyl.
1, Hydrides. 2, Formates. 3, Acetates. 4, Chlorides. 5, Bromides.

series of reactions rather than their *A* factors and activation energies. Such a comparison is made for several series of ethyl, *iso*propyl, and *tert.*-butyl esters in Fig. 2. All of these decompositions are thought to be molecular. The rate constants are corrected to 380° and are expressed in terms of the rate constant of the ethyl ester which has been assigned the value unity. In the figure the logarithms of the rate constants are plotted against the logarithms of the rate constants for the decomposition of the ethyl, *iso*propyl, and *tert.*-butyl bromides. The line labelled " hydrides " represents the rate constants for the decompositions of ethyl bromide, *n*-propyl bromide, and *iso*butyl bromide. It is evident that the same factors control the rates of each series of reactions.

We are greatly indebted to Dr. C. Barkenbus for the sample of the *tert.*-butyl formate and to the British Petroleum Company for a grant.

THE UNIVERSITY, EDINBURGH 9. [*Received, February 12th*, 1957.]

[3] Blades, *Canad. J. Chem.*, 1954, **32**, 366.

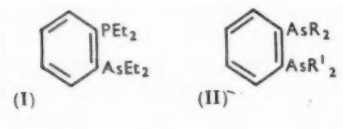
XUM

544. *The Constitution of Complex Metallic Salts. Part XVI.* The Cuprous, Argentous, and Aurous Derivatives of o-Diethylphosphinophenyldiethylarsine.*

By W. Cochran, F. A. Hart, and Frederick G. Mann.

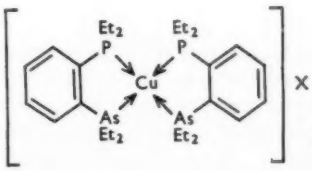
The various types of co-ordination derivatives which the di-tertiary phosphine-arsine *o*-diethylphosphinophenyldiethylarsine forms with cuprous, argentous, and aurous halides have been surveyed. Stable salts of type [(phosphine-arsine)$_2$M]I are formed only in the cuprous and aurous series. These salts should be resolvable into optically active forms, if the tetraco-ordinate metal has the tetrahedral configuration. Salts of the aurous cation with eight different optically active acid radicals gave, however, no indication of resolution. The above cuprous and aurous iodides, and the analogous aurous iodide obtained from *o*-phenylenebisdiethylarsine have therefore been examined by *X*-ray crystal analysis. They prove to be isomorphous, and the central metal atom has the tetrahedral configuration, the chelated ligand in all cases forming an angle of *ca.* 90° with the metallic atom. An explanation of the failure to resolve certain of these cuprous and aurous salts is suggested by the crystal-structure analysis.

The synthesis of *o*-diethylphosphinophenyldimethylarsine and of *o*-diethylphosphinophenyldiethylarsine (I) has been described by Jones and Mann,[1] who showed that the former acted as a strong chelating molecule with palladium bromide, giving compounds similar in type to those prepared earlier from the analogous *o*-phenylenebisdimethylarsine (II; R = R^1 = Me) by Chatt and Mann.[2]



(I)

(II)



(III)

The fully chelated derivatives of the phosphine-arsine (I) with tetraco-ordinate metals are of greater interest than those of the diarsine (II; R = R^1 = Me), since theoretically they should be capable of showing *cis–trans* isomerism if the metal has the planar configuration, or optical activity if it has the tetrahedral configuration.

We have therefore investigated the derivatives of the phosphine-arsine (I) with cuprous, argentous, and aurous halides, to see if certain of these derivatives appeared promising for optical resolution, for the quadricovalent cuprous and argentous complexes are known to have the tetrahedral configuration,[3] and there appeared to be considerable reason[4] to believe that the aurous complex also has this configuration.

We find that the phosphine-arsine (2 mols.) in ethanol readily reacts with cuprous chloride (1 mol.) in aqueous sodium chloride to give bis-(*o*-diethylphosphinophenyldiethylarsine)cuprous chloride (III; X = Cl), m. p. 211—212°. The structure of this compound is confirmed by its molar conductivity in nitrobenzene, 21·3 mhos, which is in the normal range for a uni-univalent electrolyte.

When this experiment was repeated with the phosphine-arsine (1 mol.), or alternatively

* Part XV, *J.*, 1955, 1269.

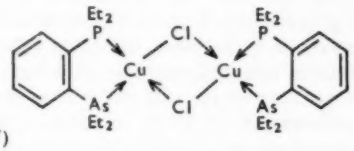
[1] Emrys R. H. Jones, and Mann, *J.*, 1955, 4472.

[2] Chatt and Mann, *J.*, 1939, 610.

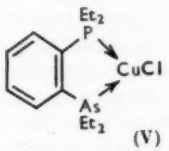
[3] Cox, Wardlaw, and Webster, *J.*, 1936, 775; Mann, Purdie, and Wells, *J.*, 1936, 1503; Mann, Wells, and Purdie, *J.*, 1937, 1828.

[4] Nyholm, *Nature*, 1951, **168**, 705; Nyholm and Stephenson, *Rec. Trav. chim.*, 1956, **75**, 687.

when the salt (III; X = Cl) was heated at 150°/0·3 mm., a compound, m. p. 194—196°, was obtained, in which the phosphine-arsine and the cuprous chloride components were in the 1 : 1 stoicheiometric ratio. The evidence for the structure of this compound follows that adduced by Kabesh and Nyholm [5] for a similar derivative of the diarsine (II; R = R^1 = Me). Our compound could be a bridged derivative (IV) or a derivative of trico-ordinate copper (V) or the dichlorocuprite of the cation in (III). The compounds (IV) and (V) would be null-valent, and our compound has a molar conductivity in nitrobenzene, 21·1 mhos, which shows it to be a uni-univalent salt, and hence the dichlorocuprite (III; X = $CuCl_2$). The molecular weight of this compound in boiling ethyl



(IV)



(V)

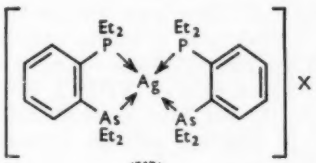
methyl ketone agreed, however, closely with that of the un-ionised salt (III; X = $CuCl_2$).

This salt underwent rapid atmospheric oxidation in hot organic solvents, and recrystallisation was performed under nitrogen. Prolonged boiling of an unprotected ethanolic solution, to promote this oxidation, gave a pale lemon-yellow crystalline compound, the analysis and molecular weight of which indicated a composition $2C_6H_4(PEt_2)(AsEt_2),3CuCl$: its solution in nitrobenzene had a molar conductivity of 25·7 mhos. It was not further investigated.

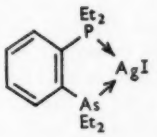
Cuprous bromide similarly gave the bromide (III; X = Br), which when heated at 100°/0·2 mm. gave the dibromocuprite (III; X = $CuBr_2$). The latter was almost insoluble in most boiling organic liquids. In boiling chloroform low values for the molecular weight were obtained, and although great accuracy cannot be claimed for these determinations owing to the very low concentration of the solutions, there is no doubt concerning the general order of the results. Their possible significance is discussed below in connection with an analogous argentous compound. The compound (III; X = $CuBr_2$) did not show ready atmospheric oxidation in solution.

Cuprous iodide also gave the iodide (III; X = I), which had greater stability than the chloride and bromide, being unaffected by heating at 100°/0·1 mm. and by even prolonged boiling of its ethanolic solution.

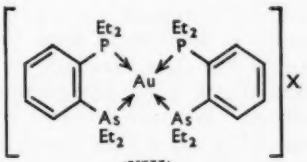
When a suspension of silver chloride in aqueous sodium chloride was vigorously shaken with the ethanolic phosphine-arsine (2 mols), only the dichloro-argentite (VI; X = $AgCl_2$) was obtained, and the instability of this compound necessitated very careful treatment to obtain it reasonably pure. In view of this factor, and the apparent non-existence of the chloride (VI; X = Cl) under our experimental conditions, further work in the argentous series was limited to the iodo-derivatives.



(VI)



(VII)



(VIII)

When a solution of silver iodide in aqueous potassium iodide was shaken with the ethanolic phosphine-arsine (2 mols.) for 3 hr., a white crystalline product, m. p. 190—230°, was obtained. A portion of this product, when treated in ethanol with an excess of

[5] Kabesh and Nyholm, *J.*, 1951, 38.

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the phosphine-arsine, gave the bis-(*o*-diethylphosphinophenyldiethylarsine)argentous iodide (VI; X = I), m. p. 158—160°, having a molar conductivity in nitrobenzene of 20·3 mhos.

A further portion, when recrystallised thrice from dimethylformamide, gave the corresponding di-iodoargentite (VI; X = AgI_2), m. p. 253—255°. It is probable therefore that the original crude product was a mixture of these two salts.

The iodide (VI; X = I) crystallises pure apparently only if the solution contains an excess of the phosphine-arsine. An ethanolic solution of the salt, moreover, even on being gently warmed, deposits the much less soluble di-iodoargentite (VI; X = AgI_2). These facts indicate strongly that in organic solvents an equilibrium may be formed: 2(VI; X = I) $\rightleftharpoons$ (VI; X = AgI_2) + $2C_6H_4(PEt_2)(AsEt_2)$. This explains the need in most solvents for an excess of the phosphine-arsine to stabilise the more soluble iodide (VI; X = I). A dilute solution of this iodide in nitrobenzene had a molar conductivity of 20·3 mhos, and gave no indication of deposition of the salt (VI; X = AgI_2).

The probable structure of the di-iodoargentite (VI; X = AgI_2) calls for comment. Its solution in nitrobenzene has a molar conductivity of 16·4 mhos, which is well below the range of the other values encountered in this investigation. In boiling chloroform it shows an apparent molecular weight of 380—390, whereas the structure (VI; X = AgI_2) requires a value of 1066. (The compound is very slightly soluble in most solvents, and the very low concentration even in boiling chloroform precluded accurate values for the molecular weight.) The explanation of these values may be that the salt in cold nitrobenzene solution exists partly as an ion-pair and is thus incompletely ionised, whereas in boiling chloroform it is completely ionised. This explanation is improbable in view of the highly ionising properties of nitrobenzene. Moreover, if it were true, the salt (VI; X = AgI_2) differs from the dichlorocuprite (III; X = $CuCl_2$), the conductivity of which in nitrobenzene indicates virtually complete ionisation, and from the dibromocuprite (III; X = $CuBr_2$), the molecular weight of which in boiling chloroform is consistent with only partial ionisation.*

An alternative explanation of our results is that the salt (VI; X = AgI_2) in solution is in equilibrium with the null-valent compound (VII), *i.e.*, (VI; X = AgI_2) $\rightleftharpoons$ 2(VII) and that the equilibrium point lies on the left-hand side in cold nitrobenzene solution, and well over on the right in boiling chloroform. The existence of the compound (VII) is not improbable, for Cass, Coates, and Hayter [6] have recently recorded stable compounds having silver iodide co-ordinated with 2 molecules of a tertiary phosphine; these compounds were monomeric in solution, the silver thus showing a co-ordination number of 3. There is at present insufficient evidence to determine the structure of compounds such as (III; X = $CuBr_2$) and (VI; X = AgI_2) when in solution. They were not further investigated as they lie outside the main line of this investigation.

Chloroauric acid, when treated in aqueous solution with an excess of the ethanolic phosphine-arsine, readily underwent reduction and co-ordination to give a colourless solution: addition of aqueous potassium iodide deposited bis-(*o*-diethylphosphinophenyldiethylarsine)aurous iodide (VIII; X = I), which readily crystallised from ethyl methyl ketone in magnificent large colourless crystals having considerable stability. Alternatively, the chloroauric acid could be co-ordinated with the phosphine-arsine and then reduced with sodium hypophosphite solution, and the more soluble chloride (VIII; X = Cl) isolated. We have prepared many salts of the cation (VIII), but have never obtained any indication of their conversion into salts comparable in structure with the dichlorocuprite (III; X = $CuCl_2$) or the di-iodoargentite (VI; X = AgI_2).

Our aurous compound (VIII; X = I) has apparently the same structure as the analogous salt which Nyholm [4] prepared from *o*-phenylenebisdimethylarsine (II;

* For a fuller discussion correlating conductivity, apparent molecular weight in solution, and structure of analogous diarsine dihalogenocuprite salts, see ref. 5.

[6] Cass, Coates, and Hayter, *J.*, 1955, 4007.

R = R^1 = Me), and which he finds by *X*-ray powder photographs to be almost certainly isomorphous with the cuprous salt prepared from this diarsine.

Of the above stable phosphine-arsine derivatives, only the cuprous and the aurous salts, (III) and (VIII) respectively, should theoretically be susceptible to optical resolution.

A brief survey of the cuprous salts (III) gave no indication of resolution, but we have investigated in considerable detail the possibility of resolving the aurous salts (VIII), particularly as they have considerable stability except in the presence of other heavy metallic ions.

The aurous iodide (VIII; X = I), when treated in aqueous ethyl methyl ketone cautiously with an aqueous solution of silver (+)-camphorsulphonate, ultimately gave the (+)-camphorsulphonate (VIII; X = $C_{10}H_{15}O_4S$); after repeated crystallisation this salt was converted into the picrate [VIII; X = $C_6H_2(NO_2)_3O$], which proved inactive. This method of double decomposition with silver salts was satisfactory, however, only if the latter were reasonably soluble in cold solvents, and consequently rapidly precipitated the silver halide: prolonged exposure of the cation (VIII) to silver salts, or (more particularly) even gentle warming of such mixtures caused decomposition of the cation by partial co-ordination of the silver with the phosphine-arsine. To avoid this difficulty, the iodide (VIII; X = I) was treated in solution with an equivalent of silver sulphate. The sulphate thus obtained proved difficult to purify, but with dilute sulphuric acid gave the crystalline hydrogen sulphate (VIII; X = HSO_4) from which, by treatment with barium hydroxide, an aqueous solution of the hydroxide (VIII; X = OH) of known concentration was obtained. Quantitative treatment of this solution with the appropriate acid gave the following crystalline salts.

(*a*) The (+)-bromocamphorsulphonate, which after ten recrystallisations from diethyl carbonate gave the inactive iodide; (*b*) the (+)-hydrogen tartrate, which gave no evidence of resolution after ten recrystallisations from ethyl methyl ketone: repeated crystallisation from water gave conversion into the (+)-tartrate, again without resolution; (*c*) the (−)-menthoxyacetate; (*d*) the (+)-camphornitronate; (*e*) the (−)-*N*-menthylphthalamate; and (*f*) the (−)-*N*-1-phenylethylphthalamate. Fractional crystallisation of the salts (*c*)—(*f*) from various solvents failed to effect resolution. The salt (*f*) appeared most promising, for fractional precipitation from acetone solution by diethyl carbonate gave a crop having $[M]_D$ +116°, increased to +128° by repeated recrystallisation from acetone: it gave however an inactive picrate [VIII; X = $C_6H_2(NO_2)_3O$]. The anomalous rotations given by various (−)-*N*-1-phenylethylphthalamate salts and the probable cause of their irregular values are discussed elsewhere.[7]

(IX) (X) (XI) (II)

In view of these failures, attempts were made to demonstrate the required dissymmetry by employing a di-arsine (II), in which the pairs of groups, R and R^1, were different.

o-Phenylene-*as*-dimethyldiphenyldiarsine (II; R = Ph, R^1 = Me) was prepared by converting *o*-bromophenyldichloroarsine (IX)[1] by phenylmagnesium bromide into *o*-bromophenyldiphenylarsine (X; R = Ph): this compound gave the lithio-derivative (XI; R = Ph) which, on treatment with iododimethylarsine, gave the required diarsine (II; R = Ph, R^1 = Me). This diarsine readily gave the bisdiarsinecopper iodide (as III; X = I) and the di-iodocuprite (as III; X = CuI_2), but did not yield a satisfactory aurous salt.

o-Phenylene-*as*-diethyldimethyldiarsine (II; R = Et, R^1 = Me) was similarly prepared in order to strengthen the co-ordinating power of the diarsine. This readily gave the

[7] Hart and Mann, following paper.

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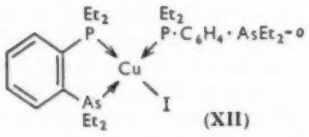
highly crystalline bisdiarsineaurous iodide, which in turn gave the corresponding (+)-camphorsulphonate and (+)-bromocamphorsulphonate: these salts crystallised with ominous readiness, and their m. p.s and rotations were unaffected by recrystallisation, which gave no evidence of resolution. The (−)-menthoxyacetate could not be obtained crystalline.

These repeated failures to obtain resolution may well have been due to mixed-crystal formation or other experimental difficulties normally attending this process. Alternatively, it is possible that the chelated ring in these spirocyclic cations may open in solution, and that, for example, the cuprous iodide (III; X = I) is in equilibrium with a minute proportion of a compound of type (XII), a process that might cause rapid racemisation if it affected the configurational stability of the copper atom in (XII). This opening of a chelated ring occurs however only when the co-ordination of one group is much weaker than that of the second group [8] and the co-ordinative power of the tertiary phosphine and arsine groups in the compound (I) are almost certainly of the same order. Moreover, no indication of such change was observed in any of our compounds, the aurous derivatives being, in the absence of other heavy metals, particularly stable.



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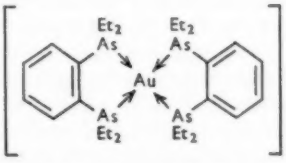
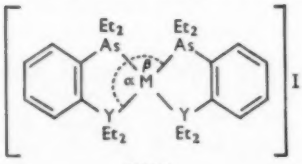


(XIII)

It became advisable however to seek decisive physical evidence that the tetraco-ordinated aurous complex was in fact tetrahedral. We have therefore prepared *o*-phenylenebisdiethylarsine (II; R = R¹ = Et) by the route outlined above. This diarsine gave the highly crystalline bis-(*o*-phenylenebisdiethylarsine)aurous iodide (XIII; X = I), which could therefore be investigated by *X*-ray crystal analysis, together with the analogous phosphine-arsine aurous iodide (VIII; X = I) and the phosphine-arsine cuprous iodide (III; X = I).

These three salts may conveniently be represented by the general formula (XIV), so that in (XIII), M = Au, Y = As; in (VIII), M = Au, Y = P; in (III), M = Cu, Y = P. The fact that these salts are all isomorphous is shown by oscillation and Weissenberg-type photographs. The central metallic atoms have a tetrahedral configuration without full tetrahedral symmetry, for in the cation (XIII), the angles $\alpha = 90° \pm 2°$, $\beta = 120° \pm 2°$, and in (III), $\alpha = 92° \pm 1{\cdot}5°$, $\beta = 119° \pm 1{\cdot}5°$. It is noteworthy that the shortest distances between iodine atoms and the gold atom range from 6·2 to 7·1 Å: these distances are too great to allow bonding between the iodine and the gold, and the latter is therefore showing without doubt a co-ordination number of four.



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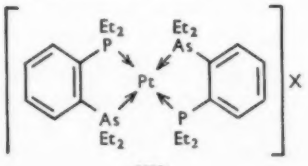

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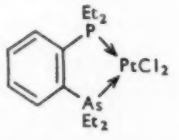

(XVI)

In the crystal structure of the compounds (VIII) and (III) an important factor arises, namely, that although the positions of the phosphorus or arsenic atoms are clearly defined, the atoms of the two elements cannot be differentiated owing to an apparently random distribution, *i.e.*, sites which for convenience we can label A and B may at one place in the crystal be occupied by phosphorus and arsenic atoms, but crystallographically equivalent sites A¹ and B¹ (related to A and B by the symmetry of the space group) may be occupied

[8] Mann and Stewart, *J.*, 1955, 1269.

by phosphorus and arsenic, or by arsenic and phosphorus, respectively. This random distribution is quite distinct from the regular arrangement to be expected in a racemate. Its occurrence might well make resolution by fractional crystallisation of a salt having an optically active anion impossible; for example, if a (+)-anion were used, there would be no physical differentiation between the (+)-cation-(+)-anion and the (−)-cation-(+)-anion, because mixed crystals would almost certainly be formed. This factor * probably accounts for our failure to resolve the phosphine-arsine cation (VIII): it is unlikely however to apply to the analogous cation prepared from the diarsine (II; R = Et, R^1 = Me).

For convenience, the conductivities obtained in the above investigation are collected in the following Table, where the symbol P-As has been used to represent the phosphine-arsine (I).

	10^4 × Concn. (M)	Conductivity (μ mho)	Λ (mho)	$\Lambda_{0\cdot005}$
$[(P\text{-}As)_2Cu]Cl$	64·5	436	21·3	22·2
$[(P\text{-}As)_2Cu][CuCl_2]$	84·6	571	21·1	23·3
$[(P\text{-}As)_2(CuCl)_2]$	31·6	259	25·7	23·9
$[(P\text{-}As)_2Ag]I$	49·4	320	20·3	20·25
$[(P\text{-}As)_2Ag][AgI_2]$	21·9	115	16·4	14·4
$[(P\text{-}As)_2Au]I$	53·5	350	20·5	20·7

In the last column, the values of Λ have been converted into $\Lambda_{0\cdot005}$, *i.e.*, the molecular conductivity at a uniform concentration of 0·005 mole/l., by using a curve based on the tabulated values obtained by Chatt [9] for a uni-univalent platinum compound. The curve can be used here with reasonable accuracy, and makes due allowance for the concentration of the solutions. The low conductivity of the $[(P\text{-}As)_2Ag][AgI_2]$ salt now becomes even more apparent in comparison with that of the other compounds.

The interaction of the phosphine-arsine (I) with sodium chloroplatinite has been briefly investigated. The chloroplatinitè, when treated in aqueous solution with the ethanolic phosphine-arsine (2 mols.) gave an immediate precipitate: the mixture, when then boiled, gave the pale salmon-pink bis-(*o*-diethylphosphinophenyldiethylarsine)platinous chloroplatinite (XV; X = $PtCl_4$), which readily crystallised from hydrochloric acid. This compound, when heated at 200°, was slowly converted into the colourless dichloro-(*o*-diethylphosphinophenyldiethylarsine)platinum (XVI). The mother-liquor from the initial preparation on evaporation gave a residue which, when recrystallised from dimethylformamide containing free phosphine-arsine, gave the colourless dichloride (XV; X = Cl_2): recrystallisation from the pure solvent caused decomposition with the formation of the null-valent compound (XVI). The cation in the salts (XV) has been depicted as the *trans*-form, solely on the basis of probability: there is at present no evidence for its configuration.

Experimental

Chemical Data.

All compounds were colourless except when otherwise stated. All rotations were determined with Na-*D* light (λ, 5893 Å).

Preparation of the Ligands.—The phosphine-arsine (I) was prepared as Jones and Mann [1] direct.

o-*Phenylene*-as-*dimethyldiphenyldiarsine* (II; R = Ph, R^1 = Me).—*o*-Bromophenyldichloroarsine [1] when treated with phenylmagnesium bromide (2 mols.) afforded, after the normal working-up, o-*bromophenyldiphenylarsine* (X; R = Ph), m. p. 101·5—103·5°, after two recrystallisations from ethanol (Found: C, 56·5; H, 3·6. $C_{18}H_{14}BrAs$ requires C, 56·1; H, 3·7%). A solution of this arsine (21·8 g.) in ether (200 c.c.) was treated under nitrogen with *n*-butyl-lithium (1 mol.) in light petroleum (b. p. 40—60°) solution (45·4 c.c.; 1·25N). After being stirred for 15 min., the mixture was treated with iododimethylarsine (13·15 g., 1 mol.) dissolved in the petroleum (100 c.c.), and then boiled for 1 hr. After hydrolysis with water and working

* It is of interest to note that a crystal of (VIII; X = I) or of (III; X = I), composed entirely of (+)-molecules, could achieve internal compensation by this same device of ignoring the difference between phosphorus and arsenic, although the optical activity would of course be manifest in solution.

[9] Chatt, *J.*, 1951, 652.

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up, the *diarsine* (II; R = Ph, R^1 = Me) was obtained initially as a crude distillate, b. p. 194—209°/1 mm. (11·0 g., 48%), which solidified on cooling, and when thrice recrystallised from ethanol had m. p. 103—104° (Found: C, 58·9; H, 5·0. $C_{26}H_{20}As_2$ requires C, 58·6; H, 4·9%).

o-*Phenylene*-as-*diethyldimethyldiarsine* (II; R = Et, R^1 = Me).—A solution of *o*-bromophenyldiethylarsine [1] (X; R = Et) (32·4 g.) in the petroleum (150 c.c.) and ether (20 c.c.) was treated as above with *n*-butyl-lithium (1 mol.) in petroleum (64·3 c.c.; 1·74N). After treatment with iododimethylarsine (26·0 g., 1 mol.) in petroleum (80 c.c.), working up gave the liquid *diarsine* (II; R = Et, R^1 = Me), b. p. 97·5—98·5°/0·15 mm. (Found: C, 46·0; H, 6·4. $C_{12}H_{20}As_2$ requires C, 45·9; H, 6·4%); 28·0 g., 80%.

o-*Phenylenebisdiethylarsine* (II; R = R^1 = Et).—This diarsine was similarly prepared by treating *o*-bromophenyldiethylarsine (10 g.) in ether (50 c.c.) with a solution of *n*-butyl-lithium (1 mol.) in the petroleum (24·3 c.c., 1·42N), and then with diethyliodoarsine (9·0 g., 1 mol.) in ether (50 c.c.). The liquid *diarsine* (II; R = R^1 = Et) had b. p. 116·5—117°/0·3 mm. (Found: C, 49·45; H, 7·0. $C_{14}H_{24}As_2$ requires C, 49·1; H, 7·1%).

Derivatives of the Phosphine-arsine (I).—*Cuprous Derivatives.*—*Bis*-(o-*diethylphosphinophenyldiethylarsine*)*cuprous chloride* (III; X = Cl). A solution of the phosphine-arsine (I) (2·61 g.) in ethanol (2 c.c.) was added to cuprous chloride (0·434 g., 1 mol. CuCl) in water (20 c.c.) containing sodium chloride (5 g.), which was shaken for 1 hr. The oily deposit which separated was collected, dried in a vacuum desiccator, and then well stirred with ethyl acetate (50 c.c.), whereupon it crystallised. The *chloride* (III; X = Cl) (2·5 g.) had m. p. 211—212°, unchanged by crystallisation from ethyl methyl ketone (Found: C, 48·4; H, 7·4. $C_{28}H_{48}ClP_2As_2Cu$ requires C, 48·3; H, 7·0%).

The dichlorocuprite (III; X = $CuCl_2$). Repetition of the above experiment, using the phosphine-arsine (5·50 g., 1 mol.) in ethanol (6 c.c.) and cuprous chloride (1·83 g., 1 mol.) in water (80 c.c.) and sodium chloride (20 g.), gave on 1 hour's shaking a solid which when collected, washed with water and dried, had m. p. 179—184°: 6·7 g. To avoid oxidation it was recrystallised rapidly from boiling ethyl methyl ketone, the solution being filtered into a vessel filled with the ketone vapour, which was replaced by nitrogen as the filtrate cooled. A second such recrystallisation gave the *dichlorocuprite* (III; X = $CuCl_2$) as very pale greenish-cream crystals, m. p. 194—196° (Found: C, 42·45; H, 6·3%; *M*, in boiling ethyl methyl ketone, 820. $C_{28}H_{48}Cl_2P_2As_2Cu_2$ requires C, 42·3; H, 6·1%; *M*, 795).

The powdered chloride (III; X = Cl) (0·4108 g.), when heated at 150°/0·3 mm. for 16 hr., furnished the dichlorocuprite (III; X = $CuCl_2$), m. p. 194·5—196° (0·2166 g.).

A solution of the crude dichlorocuprite (3·0 g.), of m. p. 175—187°, in ethanol (150 c.c.) was boiled under reflux for 7 hr. and on cooling deposited pale lemon-yellow crystals, m. p. 170—176° (slight decomp.). These crystals, when thrice recrystallised from the ketone as described above, to avoid further change, gave lemon-yellow crystals, m. p. 163—169° (preliminary sintering, slight decomp.) in an open tube, m. p. 183·5—184·5° in an evacuated tube, apparently of a di(phosphine-arsine)–tri(cuprous chloride) *complex* (Found: C, 37·8; H, 6·1; Cl, 12·6; Cu, 20·8%; *M*, in boiling 1·53% and 2·73% ethyl methyl ketone solution, 970. $2C_{14}H_{24}PAs,3CuCl$ requires C, 37·6; H, 5·4; Cl, 11·9; Cu, 21·3%; *M*, 893).

The bromide (III; X = Br). The phosphine-arsine (1·92 g., 2 mols.) in ethanol (5 c.c.) was added to cuprous bromide (0·479 g., 1 mol.) in water (20 c.c.) containing potassium bromide (10 g.), the mixture shaken for 5 min., and then evaporated to half volume to remove the ethanol. The solid which separated on cooling furnished on crystallisation from ethyl methyl ketone the *bromide hemi*(*ethyl methyl ketone*), fine needles, m. p. 181—182·5° (Found: C, 46·5; H, 7·2. $C_{28}H_{48}BrP_2As_2Cu,\frac{1}{2}C_4H_8O$ requires C, 46·4; H, 6·75%). No atmospheric oxidation was detected during the handling of this compound.

The bromide hemi-ketone complex, when heated at 35°/0·5 mm. for 14 hr., lost the ketone and then started to lose the phosphine-arsine (Found for the residue: C, 43·4; H, 6·7. $C_{28}H_{48}BrP_2As_2Cu$ requires C, 45·5; H, 6·5%). When it was heated at 100°/0·2 mm., for 36 hr., it afforded the pure *dibromocuprite* (III; X = $CuBr_2$), m. p. 222—240° (darkening) (Found: C, 38·2; H, 5·45%; *M*, in boiling 0·223% chloroform solution, 360, in 0·318% solution, 500. $C_{28}H_{48}Br_2P_2As_2Cu_2$ requires C, 38·1; H, 5·5%; *M*, 884). This salt has a low solubility in most boiling solvents, and great accuracy is not claimed for these molecular-weight determinations.

The iodide (III; X = I). This was prepared as the above bromide, the potassium bromide

being replaced by potassium iodide. The *iodide* separated after the mixture had been shaken for 5 min., and when twice recrystallised from ethyl methyl ketone gave crystals, m. p. 205·5—207·5° (Found: C, 42·85; H, 6·1. $C_{28}H_{48}IP_2As_2Cu$ requires C, 42·7; H, 6·1%). It was unaffected by heating at 100°/0·5 mm. for 10 hr., and when its ethanolic solution was boiled under reflux.

The (+)-*bromocamphorsulphonate* (III; X = $O_3S{\cdot}C_{10}H_{14}OBr$). A solution of silver (+)-bromocamphorsulphonate monohydrate (2·77 g.) in water (25 c.c.) was added slowly to one of the bromide (III; X = Br) (5·0 g., 1 mol.) in water (30 c.c.) and acetone (50 c.c.). The mixture was vigorously shaken, filtered, and evaporated in a vacuum. The residual crystalline *bromo-sulphonate* (5·8 g.), after two recrystallisations from ethyl acetate, had m. p. 155·5—157°, unchanged by further recrystallisations (Found: C, 46·7; H, 6·6. $C_{38}H_{62}O_4BrSP_2As_2Cu$ requires C, 47·0; H, 6·4%). Its solution in cold aqueous acetone, when treated with potassium iodide, deposited the optically inactive iodide (III; X = I).

The crystalline (−)-menthoxyacetate was similarly prepared, but decomposed on attempted recrystallisation from ethyl methyl ketone and other solvents.

Argentous Derivatives.—Bis-(o-diethylphosphinophenyldiethylarsine)argentous dichloroargentite (VI; X = $AgCl_2$). Solutions of silver nitrate (1·43 g., 1 mol.) in water (2 c.c.) and of the phosphine-arsine (2·42 g., 1 mol.) in ethanol (4 c.c.) were added in this order to one of sodium chloride (10 g.) in water (40 c.c.), the mixture being then shaken for 11 hr. The crude dichloroargentite when collected, washed with water, and dried, had m. p. 224—226°: 3·5 g. Recrystallisation from boiling solvents was always attended by precipitation of silver chloride. A sample of reasonable purity was obtained by recrystallising first from dimethylformamide which was heated only to 60°, and then from equal volumes of the amide and acetone, the solution being again heated to 60°, and then cooled, filtered quickly to remove silver chloride, and set aside. The *dichloro-argentite* formed compact prisms, m. p. 230·5—231·5° (decomp.) (Found: C, 38·9; H, 5·8. $C_{28}H_{48}Cl_2P_2Ag_2As_2$ requires C, 38·05; H, 5·5%). The use of 2 mols. of the phosphine-arsine in this experiment gave the same compound.

The iodide (VI; X = I). A mixture of the phosphine-arsine (5 g., 2 mols.) in ethanol (15 c.c.) and of silver iodide (2·04 g., 1 mol.) and potassium iodide (20 g.) in water (35 c.c.) was shaken for 3 hr., giving a white crystalline deposit, m. p. 190—230°: 6·5 g.

A mixture of this product and ethanol (50 c.c.), when treated with the phosphine-arsine (2 g.), gave a clear solution, which was evaporated to dryness in a vacuum desiccator. The residue, after extraction with a small quantity of cold acetone, had m. p. *ca.* 170—190°. It was dissolved in cold ethanol (10 c.c.), ethyl acetate (30 c.c.) was added, and the solution filtered from precipitated di-iodo-argentite, warmed, and filtered again, thus ensuring a slight excess of the phosphine-arsine. The filtrate on spontaneous evaporation deposited massive tablets of the *iodide* (VI; X = I), m. p. 158—162° (preliminary sintering) (Found: C, 40·4; H, 5·55. $C_{28}H_{48}IP_2AgAs_2$ requires C, 40·4; H, 5·8%).

When the above white deposit was thrice recrystallised from dimethylformamide, it afforded the *di-iodo-argentite* (VI; X = AgI_2), m. p. 253—255° (Found: C, 31·6; H, 4·6; Ag, 20·1%; *M*, in boiling 0·370% chloroform solution, 390, in 0·416% solution, 385. $C_{28}H_{48}I_2P_2Ag_2As_2$ requires C, 31·5; H, 4·5; Ag, 20·25%; *M*, 1066).

The iodide (VI; X = I), when heated at 100°/0·4 mm. for 17 hr., gave the di-iodo-argentite, m. p. and mixed m. p. 250—255°: it was pure after one recrystallisation. An ethanolic solution of the iodide when boiled readily deposited the di-iodo-argentite.

Aurous Derivatives.—Bis-(o-diethylphosphinophenyldiethylarsine)aurous iodide (VIII; X = I). (*a*) A solution of the phosphine-arsine (0·90 g., 3 mols.) in ethanol (2 c.c.), when added to chloroauric acid tetrahydrate (0·41 g., 1 mol.) dissolved in water (10 c.c.), gave an immediate yellow precipitate which dissolved on shaking to give a colourless solution containing some undissolved oily chloride (VIII; X = Cl). Sufficient ethanol was added to dissolve the chloride, and then an excess of saturated aqueous potassium iodide (*ca.* 3 c.c.), and the solution carefully diluted with water (to *ca.* 150 c.c.) to precipitate the crystalline *iodide* (0·87 g., 95%), m. p. 208—211°, increased to 212—213° by crystallisation from ethyl methyl ketone (Found: C, 36·5; H, 5·3. $C_{28}H_{48}IP_2As_2Au$ requires C, 36·5; H, 5·2%).

(*b*) The phosphine-arsine (8·3 g., 2·3 mols.) in ethanol (5 c.c.) was added to the chloroauric acid (5·0 g., 1 mol.) in water (30 c.c.), and the mixture, after vigorous shaking and cooling, was diluted with 30% aqueous sodium hypophosphite (5 c.c.), shaken for 2 hr., and set aside overnight. The precipitated chloride (VIII; X = Cl) was collected and dissolved in ethanol (20 c.c.),

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and aqueous potassium iodide cautiously added with stirring. The precipitated iodide (VIII; X = I) (8·15 g.; 73%) had m. p. 209—211·5°, increased to 212—213° by crystallisation.

Isolation of the aurous cation as the chloride is wasteful, for this salt is more soluble than the iodide, and crystallises poorly in the presence of impurities. The precipitated chloride (above), when recrystallised from ethyl methyl ketone, gave the pure *chloride hemi-ketone complex*, m. p. 224—230° (decomp.) (Found: C, 41·5; H, 6·2. $C_{28}H_{46}ClP_2As_2Au,\frac{1}{2}C_4H_8O$ requires C, 41·55; H, 6·1%), which when heated at 60°/0·05 mm. for 8 hr. gave the solvent-free *chloride*, of unchanged m. p. (Found: C, 40·2; H, 5·7. $C_{28}H_{46}ClP_2As_2Au$ requires C, 40·6; H, 5·8%).

This salt in ethanol readily gave the *picrate* [VIII; X = O·$C_6H_2(NO_2)_3$] yellow crystals, m. p. 118—120°, from aqueous methanol (Found: C, 40·2; H, 4·8; N, 4·25. $C_{34}H_{50}N_3O_7P_2As_2Au$ requires C, 40·0; H, 4·9; N, 4·1%).

The hydrogen sulphate (VIII; X = HSO_4). A solution of silver sulphate (1·39 g.) in water (170 c.c.) was added slowly to a well-stirred solution of the iodide (VIII; X = I) (8·23 g., 2 mols.) in acetone (110 c.c.). The complete mixture was shaken for 1 min., filtered, and evaporated to dryness under reduced pressure. The residual sulphate, which could not be induced to crystallise, was converted into the hydrogen sulphate by crystallisation first from water (150 c.c.) containing concentrated sulphuric acid (0·5 c.c.), giving fine needles (5·55 g., 68%), and then in turn again from very dilute sulphuric acid and from water. The needles, when dried over phosphoric oxide in a vacuum-desiccator, gave the *hydrogen sulphate monohydrate*, m. p. 214—216° on slow heating, but immediately melting with effervescence on immersion at 200° (Found: C, 37·0; H, 5·6. $C_{28}H_{49}O_4SP_2As_2Au,H_2O$ requires C, 37·05; H, 5·7%). A solution of this salt in dilute sulphuric acid deposits a film of gold on the walls of the containing vessel when set aside for some weeks.

When aqueous solutions of the hydrogen sulphate and of barium hydroxide (1 mol.) were mixed, filtered, and evaporated to dryness under reduced pressure at room temperature, a crystalline residue, almost certainly the hydroxide (VIII; X = OH) was obtained. Recrystallisation was achieved only from diethyl carbonate, which afforded crystals, m. p. 222—224° (preliminary darkening), the composition of which indicated the formation of either a carbonate trihydrate or a hydrogen carbonate dihydrate (Found: C, 38·9; H, 6·0. $C_{57}H_{98}O_3P_4As_4Au_2,3H_2O$ requires C, 39·0; H, 6·2%. $C_{29}H_{49}O_3P_2As_2Au,2H_2O$ requires C, 39·1; H, 6·0%).

In the resolution experiments described below [except (i) and (v)], a freshly prepared solution of the hydroxide of known concentration was therefore neutralised directly by the appropriate acid to obtain certain salts.

Attempted Resolution of the Bis-(o-diethylphosphinophenyldiethylarsine)aurous Cation (VIII).—(i) A solution of silver (+)-camphorsulphonate (0·386 g.) in water (5 c.c.) was slowly added to a well-stirred solution of the iodide (VIII; X = I) (1 g., 1 mol.) in water (20 c.c.) and ethyl methyl ketone (25 c.c.). The filtered solution was evaporated to dryness under reduced pressure, and the residual *sulphonate* (VIII; X = $O_3S{\cdot}C_{10}H_{15}O$) when twice recrystallised from the ketone had m. p. 225—226°, unchanged by further crystallisation (Found: C, 44·9; H, 6·1. $C_{38}H_{63}O_4SP_2As_2Au$ requires C, 44·5; H, 6·2%). It was converted into the picrate, which was inactive in ethanolic solution.

(ii) Barium hydroxide solution was carefully added to a solution of the hydrogen sulphate (VIII; X = HSO_4) (15 g.) in ethanol (15 c.c.) and water (30 c.c.) until the addition of a further few drops to the filtered solution gave no further cloudiness. An aqueous solution of (+)-bromocamphorsulphonic acid (1 mol.) was now added, and the solution evaporated to dryness under reduced pressure. The *bromo-sulphonate* (VIII; X = $O_3S{\cdot}C_{10}H_{14}OBr$) had m. p. 165—165·5° after 2 and after 10 recrystallisations from diethyl carbonate (Found: C, 41·6; H, 5·35. $C_{38}H_{62}O_4BrSP_2As_2Au$ requires C, 41·4; H, 5·7%). A solution of the final product (0·4272 g.) in ethanol (10 c.c.) which was then made up to 30 c.c. with water had [*M*] +306°. A solution of the silver sulphonate (0·2508 g.) in this volume of the mixed solvents had [*M*] +292°. The sulphonate was converted into the inactive iodide.

(iii) The solution of the hydroxide (VIII; X = OH), prepared as in (ii), was treated with a solution of tartaric acid (2·53 g., 1 mol.) in water (10 c.c.), and evaporated to *ca.* 70 c.c. under reduced pressure at 60°. The *hydrogen tartrate* (VIII; X = $C_4H_5O_6$) (13·3 g., 84%) crystallised on cooling, and when collected, washed with water, and dried over phosphoric oxide, had m. p. 188—190·5° (immersed at 180°): after four recrystallisations from water, it had m. p. 187—189° (Found: C, 41·1; H, 5·95. $C_{32}H_{53}O_6P_2As_2Au$ requires C, 40·8; H, 5·7%). A sample was

recrystallised ten times from ethyl methyl ketone, and then had m. p. 188·5—190° : the rotation in ethanol changed from $[M]$ +33° to +29° during this process. The final product gave an inactive picrate.

This salt, when recrystallised 9 times from water gave the (+)-*tartrate monohydrate*, m. p. 185—187° on slow heating to ensure preliminary dehydration, 140° (efferv.) when immersed at 130° (Found : C, 40·55; H, 5·8. $C_{60}H_{100}O_6P_4As_4Au_2,H_2O$ requires C, 40·7; H, 5·9%). A solution of this salt (0·2125 g.) in ethanol (30 c.c.) had $[M]$ +89°. One recrystallisation from aqueous tartaric acid regenerated the hydrogen tartrate. The distinction between the two tartrates was confirmed by (*a*) a mixture of the two salts when slowly heated showed a depression in m. p., (*b*) aqueous solutions were acidic and neutral respectively.

(iv) A solution of the hydroxide, treated with (−)-menthoxyacetic acid (1 mol.) and then evaporated in a vacuum desiccator gave ultimately a sticky solid, which when stirred thoroughly with cold ethyl acetate afforded the very deliquescent crystalline (−)-*menthoxyacetate* (VIII; X = $C_{12}H_{21}O_3$), m. p. 171·5—173·5°, unchanged by 3 recrystallisations from ethyl acetate–*cyclo*hexanone (10 : 1 by vol.) (Found : C, 47·9; H, 7·0. $C_{40}H_{69}O_3P_2As_2Au$ requires C, 47·7; H, 6·9%). The nature and quantity of this salt precluded further crystallisation. It was converted into the inactive iodide.

(v) A solution of sodium (+)-camphornitronate (5·3 g.; 5 mols.) in water (15 c.c.), when added with stirring to one of the chloride (VIII; X = Cl) (4·0 g.) in water (20 c.c.) and ethanol (5 c.c.), deposited a sticky product which, when collected, washed with water, dried, and washed with ethyl acetate, gave a powder, m. p. 158—168° : 3·6 g. This was recrystallised thrice from ethyl methyl ketone, in which it was markedly soluble, and twice from ethyl acetate–ethyl methyl ketone. The (+)-*camphornitronate* (VIII; X = $C_{10}H_{14}O_3N$) then had m. p. 173—182° (Found : C, 46·0; H, 6·5; N, 1·6. $C_{38}H_{62}O_3NP_2As_2Au$ requires C, 46·1; H, 6·3; N, 1·4%) : it gave an inactive iodide.

(vi) The (−)-menthylphthalamate was prepared as in (ii) and obtained as an oil which crystallised only on exposure to moist air for 5 days. This salt in contact with most solvents either dissolved readily, or became an oil. Spontaneous evaporation of a 10% solution in diethyl carbonate, containing just sufficient acetone to give complete initial dissolution, gave large tablets of the (−)-*menthylphthalamate* (VIII; X = $C_{18}H_{24}O_3N$), m. p. 86·5—88·5° (immersed at 80°) after 2 and 6 such crystallisations (Found : C, 50·6; H, 7·0; N, 1·3. $C_{46}H_{72}O_3NP_2As_2Au$ requires C, 50·4; H, 6·6; N, 1·3%). The final crop gave an inactive complex picrate.

(vi) The (−)-N-1-*phenylethylphthalamate* was prepared by neutralising the hydroxide with the phthalamic acid. The oily product would not crystallise if kept dry, but slowly crystallised when exposed to the air for several days in contact with diethyl carbonate. The salt could not be recrystallised at this stage, and it was therefore precipitated from its acetone solution by the addition of diethyl carbonate, and then had $[M]$ +116° in 3·106% ethanolic solution. The salt, when now recrystallised from acetone, had m. p. 108—110° (efferv.), unchanged by further recrystallisations. After 2 and 4 such recrystallisations, the salt had $[M]$ +125° (2·603% solution) and +128° (1·039% solution) respectively (Found : C, 49·6; H, 5·85; N, 1·3. $C_{43}H_{61}O_3NP_2As_2Au$ requires C, 49·8; H, 5·9; N, 1·3%). The final crop, treated in ethanolic solution with sodium picrate, gave the inactive picrate.

Derivatives of o-*Phenylene*-as-*dimethyldiphenyldiarsine* (II; R = Me, R¹ = Ph).—A solution of the diarsine (0·5 g., 4 mols.) in acetone (5 c.c.) was added to one of cuprous iodide (0·1164 g., 1 mol.) in water (2 c.c.) containing potassium iodide (4 g.), and the mixture shaken for 6 hr. The solid product was collected, washed with boiling water, and recrystallised from ethanol. The hot filtered solution rapidly deposited small hard highly insoluble crystals (*ca.* 0·05 g.) of *bis*-(o-*phenylene*-as-*dimethyldiphenyldiarsine*)*cuprous di-iodocuprite* (as III; X = CuI_2), m. p. 214—215·5° after washing with ethanol and acetone (Found : C, 40·0; H, 3·2. $C_{40}H_{40}I_2As_4Cu_2$ requires C, 40·0; H, 3·4%). When this deposition was complete, the hot solution was filtered, and on cooling gave the *iodide* (as III; X = I) (0·35 g.), m. p. 179·5—180·5° after recrystallisation from ethanol (Found : C, 48·1; H, 3·9. $C_{40}H_{40}IAs_4Cu$ requires C, 48·5; H, 4·1%). This iodide slowly turns green when exposed to air : its ethanolic solution when boiled slowly deposits the di-iodocuprite.

The insolubility of the first product prevented an investigation of its structure, and it is classed as a di-iodocuprite solely in harmony with the other halogenocuprites which have arisen in this investigation.

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The iodide was converted into the (+)-bromocamphorsulphonate, an oil which could not be induced to crystallise.

Derivatives of o-*Phenylene-as-diethyldimethyldiarsine* (II; R = Me, R^1 = Et).—*Aurous derivatives.* The *bis-diarsine-aurous iodide* (as XIII; X = I) was prepared exactly as the "phosphine-arsine" salt, by the sodium hypophosphite method, and obtained as crystals, m. p. 157—157·5°, when recrystallised from ethyl methyl ketone (Found: C, 30·3; H, 4·4. $C_{24}H_{40}IAs_4Au$ requires C, 30·2; H, 4·2%).

Solutions of this iodide (1 g.) in acetone and of silver (+)-camphorsulphonate (0·356 g., 1 mol.) in water (5 c.c.) were mixed, shaken, filtered, and evaporated to dryness in a desiccator. The residual *sulphonate* (as XIII; X = $O_3S{\cdot}C_{10}H_{15}O$), after three recrystallisations from diethyl carbonate, had m. p. 184·5—186° (Found: C, 38·85; H, 5·35. $C_{34}H_{55}O_4SAs_4Au$ requires C, 38·6; H, 5·2%). A solution of the final crop (0·2933 g.) in ethanol (5 c.c.) made up to 30 c.c. with water had [*M*] +54°: this rotation is that of the sulphonate ion alone.[10]

The (+)-bromocamphorsulphonate (as XIII; X = $O_3SC_{10}H_{14}OBr$) was similarly prepared, and after one crystallisation from ethyl acetate had m. p. 175—177·5°, unchanged by further crystallisation (Found: C, 35·9; H, 5·05. $C_{34}H_{54}O_4BrSAs_4Au$ requires C, 35·95; H, 4·8%). It gave an optically inactive picrate.

The (−)-menthoxyacetate was obtained by neutralisation of the complex hydroxide, but could not be induced to crystallise.

Bis(o-*phenylenebisdiethylarsine*)*aurous salts* (XIII). Sodium chloroaurate in aqueous solution was treated with the ethanolic diarsine (2·2 mols.) and then with sodium hypophosphite, as described for the bis-phosphine-arsine salt. The solution was diluted with ethanol until clear and then divided into two portions. One portion, when treated with aqueous sodium bromide, deposited crystals, which when recrystallised from ethyl methyl ketone gave the *bromide hemi*(*ethyl methyl ketone*) *complex*, m. p. 181—182° (Found: C, 36·5; H, 4·7. $C_{28}H_{48}BrAs_4Au,\frac{1}{2}C_4H_8O$ requires C, 36·1; H, 5·25%). This compound, when heated at 60°/0·2 mm. for 8 hr., gave the solvent-free *bromide* (XIII; X = Br), of unchanged m. p. (Found: C, 34·8; H, 5·0. $C_{28}H_{48}BrAs_4Au$ requires C, 35·0; H, 5·0%).

The second portion, treated with aqueous potassium iodide, gave the *iodide* (XIII; X = I), m. p. 166—167° after crystallisation from ethyl methyl ketone (Found: C, 33·2; H, 4·7. $C_{28}H_{48}IAs_4Au$ requires C, 33·35; H 4·8%).

It will be noted that ethyl methyl ketone proved to be the most useful solvent for many of the salts isolated in this investigation. Furthermore, whereas the chlorides and bromides of the cuprous cation (III) and the aurous cations (VIII) and (XIII) often crystallised with half a molecule of the ketone, the crystalline iodides were always solvent-free.

Platinous Derivatives of the Phosphine-arsine (I).—A solution of the phosphine-arsine (1·26 g., 2 mols.) in ethanol (1·5 c.c.) when added to one of sodium chloroplatinite (0·81 g., 1 mol.) in water gave an immediate precipitate, but the mixture after shaking for 30 min. was still red and smelt of the arsine. Ethanol (25 c.c.) was added, and the solution boiled under reflux for 10 min., and the deposited pale salmon-pink *bis*-(o-*diethylphosphinophenyldiethylarsine*)*platinous chloroplatinite* (XV; X = $PtCl_4$), when collected, twice recrystallised from concentrated hydrochloric acid diluted with an equal volume of water, and dried, on heating became white at *ca.* 250—260° but did not melt below 310° (Found: C, 30·2; H, 4·3. $C_{28}H_{48}Cl_4P_2As_2Pt_2$ requires C, 29·8; H, 4·3%).

This salt, when heated at 220°/760 mm. for 18 hr., gave the *dichloro*(*phosphine-arsine*)-*platinum* (XVI), separating from dimethylformamide as colourless crystals, unmelted at 310° (Found: C, 29·5; H, 4·6. $C_{14}H_{24}Cl_2AsPPt$ requires C, 29·8; H, 4·3%).

The mother-liquor from which the crude chloroplatinite had separated was evaporated almost to dryness under reduced pressure, and gave a residue, m. p. 244—246°: 0·7 g. This product, when recrystallised from dimethylformamide, was steadily converted into the compound (XVI): recrystallisation from the amide containing much free phosphine-arsine gave the pure *dichloride* (XV; X = Cl_2), m. p. 258·5—261·5° (Found: C, 38·7; H, 5·8. $C_{28}H_{48}Cl_2P_2As_2Pt$ requires C, 38·9; H, 5·6%).

Crystallographic Data.

The bis(diarsine)aurous iodide (XIII; X = I), the bis-(phosphinearsine)aurous iodide (VIII; X = I), and the bis(phosphine-arsine)cuprous iodide (III; X = I) have been investigated by *X*-ray diffraction methods: a general representation of these compounds is given in (XIV) (p. 2820).

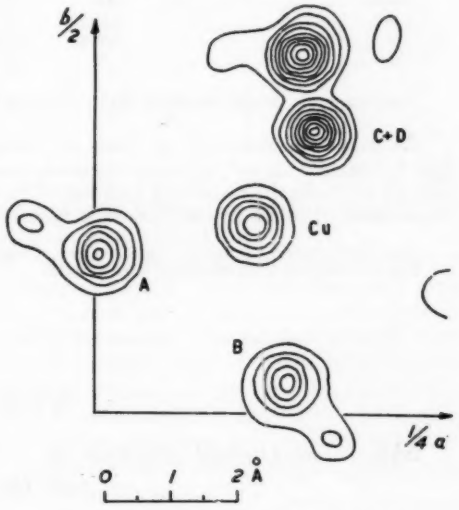
[10] Graham, *J.*, 1912, **101**, 746.

Photographs were taken with use of Cu and also Mo characteristic radiations. Oscillation and Weissenberg-type photographs showed the three compounds to be isomorphous, with orthorhombic unit cells having a, b, and c dimensions (Å) as follows: (XIII) 21·7, 11·6, 14·1; (VIII) 21·7, 11·3, 13·7; (III) 21·5, 11·4, 13·5. These values have an estimated standard deviation of 0·7%.

There were no systematic absences among the general reflections. Zero-layer Weissenberg photographs showed the following systematic absences:

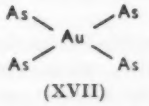
Zone (010); $F(h0l) = 0$ for h odd, $F(00l) = 0$ for l odd
Zone (001); $F(h00) = 0$ for h odd, $F(0k0) = 0$ for k odd

These absences establish the space group as $Pna2_1$ (No. 33) or $Pnam$ (No. 62). The systematic absences in the (100) zone, which was not investigated, would not serve to distinguish these two possibilities. Space group $Pnam$ would require a molecular plane of symmetry or centre of symmetry, with metal and iodine ions occupying special positions. The X-ray intensities rule out this possibility, and the structure analysis has proceeded satisfactorily on the assumption that the space group is $Pna2_1$, with four formula units per unit cell [calculated density for (XIII) = 1·89 g. c.c.].



The compound (III; X = I). *Electron-density projected on* (001). *Approximately half the unique area is shown. Contours are drawn at an equal (arbitrary) interval.*

The Patterson function projected on planes (001) and (010) has been calculated for (XIII), and the corresponding projection on (001) for (III). From these the approximate co-ordinates of the heavier atoms could be found, and the signs of most of the ($hk0$) structure factors calculated. Essentially the same set of signs was found by the EDSAC method.[11] Projections of the electron density on (001) have been calculated for (XIII) and for (III); part of the latter, showing the arrangement of the heavier atoms, is shown in the Figure. The refinement of the two structures has not yet been carried beyond the stage where bond lengths and angles involving the heavier atoms are established with standard deviations of about 0·03 Å and 1·5° respectively. It is in fact doubtful whether it will ever be possible to establish the positions of the carbon atoms with worthwhile accuracy. The following points concerning the stereochemistry of the molecule are however well established: in the compound (XIII) the group



(XVII)

(XVII) has tetrahedral symmetry (point group symmetry $\bar{4}2m$) within the present limits of experimental error. The Au–As bonds are of length 2·48 ± 0·04 Å, there are two bond angles of 90° ± 2° and four of 120° ± 2°. There is no question of an approach to five-fold co-ordination around the gold atom, the four nearest iodine atoms to any gold atom being at distances ranging from 6·2 to 7·1 Å.

[11] Cochran and Douglas, *Proc. Roy. Soc.*, 1955, *A*, **227**, 486.

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For compound (III) the results are consistent with the assumption that the arrangement of bonds around the cuprous atom also has symmetry $\bar{4}2m$. The equality of the peaks A and B (Figure), and the fact that the peak C + D is approximately twice the height of either, shows that arsenic and phosphorus atoms are not distinguished in the crystal structure. This does not conflict with the chemical evidence that a benzene ring always bridges one phosphorus and one arsenic atom; it merely indicates that if an arsenic atom occupies site A in one unit cell and is bridged by a benzene ring to a phosphorus atom in site B, in a neighbouring unit cell it is just as likely that a phosphorus atom occupies site A with an arsenic atom in site B. The bond length and angles corresponding to those given above are 2·38 ± 0·03 Å, 92° ± 1½° and 119° ± 1½°. Small peaks representing single carbon atoms do not show in the electron-density map at the present stage of refinement, but the peaks of moderate height immediately adjacent to A and to B (Figure) must each represent two $\cdot CH_2 \cdot CH_3$ groups with all four carbon atoms nearly superimposed in projection. The positions of these peaks indicate that a benzene ring bridges atoms A and B, and another bridges C and D. This is as would be expected from the fact that it is the angles ACuB and CCuD which equal 92°.

Approximate atomic co-ordinates in (XIII)

Atom	As[1]	As[2]	As[3]	As[4]	Au	I
x/a	0·133	0	0·153	0·153	0·108	0·150
y/b	0·038	0·194	0·374	0·374	0·243	0·475
z/c	0	0	0·126	−0·126	0	0·500

Further work should establish more accurate bond lengths and angles.

We thank Dr. Emrys R. H. Jones for a supply of *o*-diethylphosphinophenyldiethylarsine, Mrs. S. Osmond for her help with the measurement of *X*-ray intensities, Dr. M. V. Wilkes for making available the computing facilities of the Cambridge Mathematical Laboratory, and the Department of Scientific and Industrial Research for a grant (to F. A. H.).

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NOTES.

545. *The Optical Rotation of* (−)-N-1-*Phenylethylphthalamic Acid and Its Salts.*

By F. A. HART and FREDERICK G. MANN.

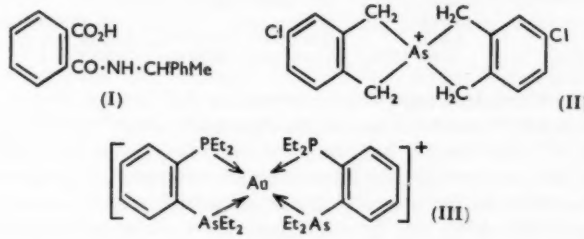
THE above acid (I) can be readily prepared by the interaction of phthalic anhydride and (−)-1-phenylethylamine in boiling ether, and Mann and Watson [1] record $[M]$ −130° for a 0·559% ethanolic solution. (All rotations are measured with the Na_D light, λ 5893 Å.) The acid should be of considerable value for the optical resolution of bases and appropriate salts, particularly as the (+)-acid is also available. The object of this Note is to point out that the progress of the resolution of a cation by the fractional crystallisation of its phenylethylphthalamate cannot be reliably assessed by the rotation of the salt. This is due to the fact that the order and sign of the rotation of the phthalamate ion depend both on the concentration of the solution and on the nature of the associated cation, even when the latter is itself symmetric.

This first became apparent during attempts to resolve the *As-spiro*-bis-5-chloro*iso*-arsindolinium cation (II),[2] the (−)-1-phenylethylphthalamate of which, when once recrystallised from ethanol, had no detectable activity in 0·65% ethanolic solution, and

[1] Mann and Watson, *J.*, 1947, 505.
[2] Lyon, Mann, and G. H. Cookson, *J.*, 1947, 662.

when twice recrystallised had [α] +2·7°, [*M*] +17° in 0·660% solution. The cation (II) in this crop was precipitated as the thiocyanate, which was inactive. In another preparation the phthalamate was recrystallised three times from ethanol, and then was again apparently inactive in 0·511% ethanolic solution. This crop when treated in ethanolic solution with picric acid deposited the arsindolinium picrate, which was inactive, but the mother-liquor showed the (−)-rotation expected of the free phthalamic acid. The reasonable deduction to draw from the optical inactivity of a salt of an optically active acid, namely, that the cation had an activity equal and opposite to that of the anion, is invalid in this case.

A more striking example is that of the (−)-*N*-1-phenylethylphthalamate of the bis-(*o*-diethylphosphinophenyldiethylarsine)aurous cation [3] (III), the initial crop of which, and



the crops obtained after two and four recrystallisations, had [α] +10·9°, +11·7°, +12·0°, [*M*] +116°, +125°, and +128° in 3·106, 2·603, and 1·039% ethanolic solutions respectively. The final crop gave however the inactive picrate of the cation (III).

We have therefore briefly investigated the sodium, ammonium, and potassium salts of the acid (I). These salts were not readily recrystallised in small quantities, and were therefore prepared by careful addition of the ethanolic base (1 mol.) to a cold ethanolic solution of the acid, which was then evaporated to dryness in a vacuum-desiccator at room temperature. The salts had the rotations: Na salt, 1·340% ethanolic solution, [α] +0·56°, [*M*] +1·6°; NH_4 salt, 1·78% solution in aqueous ethanol (13 : 87 by vol.), [α] −3·65°, [*M*] −10·5°; K salt, 1·3999 and 4·197% ethanolic solutions, [α] −13·8° and −21·3°, [*M*] −42° and −66° respectively. The rotation of the potassium salt solution remained unchanged when set aside for 24 hr. at room temperature. The rotations of these salts cannot be affected by asymmetric transformation in solution.

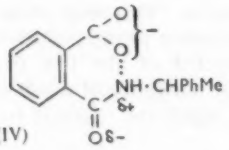
Although a change in the order or even in the sign of the rotation of a compound with change in concentration is not uncommon (cf. 2-amino-*n*-octane hydrochloride [4]), it is unusual for such a change in the rotation of an ion to be caused by the nature of the opposite ion. We suggest tentatively that in the phthalamate ion the slight positive charge on the nitrogen atom (which is normal for amide groups) may cause an appreciable electrostatic attraction between this atom and the negative oxygen of the carboxylate ion (IV). The rotation of this " bonded " ion would very probably be different from that of the unbonded ion. It is highly probable that in solution an equilibrium would exist between these two forms, and the rather delicate electronic equilibrium which determines this would almost certainly be affected by the concentration of the solution, and by the size and nature of the cation, *i.e.*, by the intensity of the positive charge on the periphery of the cation.

An alternative explanation, namely, that the positive charge on the nitrogen atom and the consequent increase in the acidic nature of the hydrogen atom to which it is attached may promote hydrogen bonding (V), and that the equilibrium in solution is between this

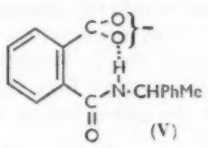
[3] Cochran, Hart, and Mann, preceding paper.
[4] Mann and Porter, *J.*, 1944, 456.

XUM

" bonded " ion and the unbonded ion, receives little support from the infrared spectrum of the carefully dried potassium salt. Dr. N. Sheppard reports : " The spectrum of this



(IV)



(V)

salt showed the following absorption bands (cm.$^{-1}$) which could be correlated with the presence of functional groups.

(*a*) $-CO\cdot NH-$	3240	NH stretching frequency
	1640	C=O ,, ,, in amide (amide I)
	1568	NH deformation frequency (amide II)
(*b*) $-CO_2^-$	1590, 1384	Stretching vibrations of this ion

A particularly strong hydrogen bond between the NH linkage of the amide group and the $\cdot CO_2^-$ group would be expected to give an abnormally low NH stretching frequency and perhaps a high NH deformation frequency for the $\cdot CO\cdot NH\cdot$ group. The NH stretching frequency is in fact just outside the lower limit of the generally accepted range for this vibration (3320—3270 cm.$^{-1}$) ; [5] the NH deformation frequency is towards the high end of the usual range (1570—1515 cm.$^{-1}$).[5] Although these observations do suggest that the NH bond is rather more strongly hydrogen-bonded than is usual in amides, the effect is not marked. The possibility cannot be ruled out that the hydrogen bonding present is that of the ordinary amide-to-amide intermolecular type rather than that of the intramolecular type (V). The spectrum of the sodium salt is virtually identical with that of the potassium salt throughout the above regions."

Experimental.—Salts of the (−)-*acid* (I). The potassium salt, prepared as above, formed deliquescent crystals, which were dried at 50°/0·01 mm. The sample used for the infrared spectrum determination was handled in a dry-box immediately after drying, and the spectrum indicated the presence of only traces of water. The elementary analysis of another portion of this sample indicated the presence of a hemihydrate, although this may have been fortuitous, in spite of the precautions taken during the analytical manipulation (Found : C, 60·5, 60·8; H, 4·7, 4·9; N, 4·4. Calc. for $C_{16}H_{14}O_3NK$: C, 62·5; H, 4·6; N, 4·6. $C_{16}H_{14}O_3NK,\frac{1}{2}H_2O$ requires C, 60·7; H, 4·7; N, 4·4%). The *sodium salt*, similarly prepared and dried, was not deliquescent (Found : C, 65·2; H, 5·0; N, 4·8. $C_{16}H_{14}O_3NNa$ requires C, 65·8; H, 4·8; N, 4·8%).

We thank the Department of Scientific and Industrial Research for a grant (to F. A. H.).

THE UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, January 22nd*, 1957.]

[5] Bellamy, " The Infra-Red Spectra of Complex Molecules," Methuen, London, 1954, p. 176.

546. *Compounds of Silicon. Part II.* The Reaction of Silicon Halides with Diazoalkanes.*

By R. A. Shaw.

The diazo-alkane method of alkylenation has been successfully employed with silicon tetrachloride and tetrabromide, methyltrichlorosilane,[1] and trichlorosilane,[2] $SiX_4 + CHRN_2 \longrightarrow SiX_3{\cdot}CHRX + N_2$, but with silicon tetrafluoride,[1] triethyl-,[1] trimethyl-,[2] and triphenyl-chlorosilane,[2] and tetraethoxysilane [2] it failed to give the desired organosilicon products. Yakubovich and his co-workers [1] suggested a free-radical mechanism involving initial formation of an alkylene biradical CHR:, which then attacked the silicon–halogen bond. Seyferth [3] prefers a polar mechanism, pointing out that all metals whose halides undergo alkylenation possess available *d*-orbitals, and that a primary co-ordination step is possible.

The present work agrees with the latter mechanism. Whilst silicon tetrachloride with diazomethane in ether with or without a copper catalyst gave chloromethyltrichlorosilane in reasonable to good yields (with boron trifluoride as catalyst only " polymethylene " was obtained), reaction in *n*-pentane was much slower and yielded only " polymethylene." The solvating power of the medium therefore exerts a powerful effect on the rate as well as on the course of this reaction. Strong inhibition of a free-radical reaction would not be expected on passing from a polar to a non-polar solvent (provided no interaction with the solvent took place), whilst reduction in rate, or complete suppression, of a heterolytic reaction in the latter solvent is acceptable.

The increase in steric screening in the series SiX_4, $SiRX_3$, SiR_2X_2, SiR_3X invoked by Yakubovich and his co-workers to account in part for the slower alkylenation [1] and hydrolysis in this series, is hardly applicable as the larger chloro- and bromo-methyl derivatives are much more reactive towards diazomethane than are the corresponding methyl compounds. The reason for the smaller reactivity of, *e.g.*, methyltrichlorosilane than of trichlorochloromethylsilane towards diazomethane arises therefore from the greater electron-density on the silicon atom in the former compound, which hinders the approach of a nucleophilic reagent.[3] Further evidence for the polar mechanism is the reaction of trichlorosilane with diazomethane,[2] which gives dichlorochloromethylsilane (*i.e.*, reaction of a Si–Cl bond) in excellent yield : in well-established free-radical reactions trichlorosilane suffers fission of its Si–H bond when it adds to olefins,[4] perfluoro-olefins,[5] or acetylenes.[6]

The homopolar and " ionic bond energies " [7] of the Si–X bonds discussed, explain many of the reported results. Whilst these figures (see Table) cannot be considered strictly quantitative, and do not permit comparisons between the two types of bond energies (because of the effects of the other groups attached to the silicon atom, and because of solvation effects), within each type they provide a reasonable qualitative order of the energies required to heterolyse or homolyse Si–X bonds. Thus whilst Si–C and Si–H bonds are weaker than the Si–Cl bond, their " ionic bond energies " are much greater than

* Part I, *J.*, 1956, 2779.

[1] Yakubovich, Makarov, Ginsburg, Gavrilov, and Merkulova, *Doklady Akad. Nauk S.S.S.R.*, 1950, **72**, 69; *Chem. Abs.*, 1951, **45**, 2865; Yakubovich and Ginsburg, *Zhur. obshchei Khim.*, 1952, **22**, 1783; *Chem. Abs.*, 1953, **47**, 9256.

[2] Seyferth and Rochow, *J. Amer. Chem. Soc.*, 1955, **77**, 907.

[3] Seyferth, *Chem. Rev.*, 1955, **55**, 1155.

[4] Sommer, Pietrusza, and Whitmore, *J. Amer. Chem. Soc.*, 1947, **69**, 188; Barry, DePree, Gilkey, and Hook, *ibid.*, p. 2966.

[5] Haszeldine and Marklow, *J.*, 1956, 962.

[6] Burkhard and Krieble, *J. Amer. Chem. Soc.*, 1947, **69**, 2687.

[7] Eaborn, *J.*, 1950, 3077.

XUM

that of the Si–Cl bond, and thus the lack of methylenation of the Si–H bond in trichlorosilane,[2] and of the Si–C bond in, *e.g.*, methyltrichlorosilane,[1] as well, of course, as of the Si–O bond in tetraethoxysilane,[2] is readily explained.

Bond Si–X	Homopolar bond energy (kcals.) [9]	" Ionic bond energy " (kcals.) *	Bond Si–X	Homopolar bond energy (kcals.) [9]	" Ionic bond energy " (kcals.) *
Si–I	55·0	167·4	Si–C≡	75·0	222·9
Si–Br	73·5	179·0	Si–F.....	134·0	237·4
Si–Cl	90·3	190·3	Si–O–	106·0	242·4
Si–S–	60·9	192·7	Si–H	79·9	249·8

* Calc. from electron affinities given by Pritchard and Skinner.[9]

The reaction of trimethylchlorosilane with 9-diazofluorene has been investigated in the presence of copper bronze in ether and pyridine solutions. From the ether solution only di-9-fluorenylidene was isolated, but when pyridine was used in the hope that the more polar solvent would facilitate Si–Cl heterolysis dipyridinecupric chloride [10] and fluorenone azine were obtained. Karrer and his co-workers [11] have reported that organic and inorganic acid chlorides dissolve copper bronze at room temperature on addition of dry pyridine in a few seconds, the above-mentioned copper derivative being one of the products. This reaction provides yet another example of the similar chemical behaviour of silicon and acyl halides.[12]

Experimental.—A column of approx. six theoretical plates was employed for fractional distillation.

Ether and *n*-pentane for dissolving the silicon halides (fractionally distilled before each experiment) were dried with sodium wire. The pyridine was dried first over potassium hydroxide and then by azeotropic distillation.

Diazomethane was prepared in ether or *n*-pentane from methylnitrosourea,[13] dried, and standardised.[3]

Unless otherwise stated, yields of halogenoalkylsilanes are based on diazomethane.

Reactions of silicon tetrachloride with diazomethane. (*a*) Silicon tetrachloride (82 g., 0·48 mole) in ether (100 ml.) was cooled to −50° and diazomethane (10·9 g., 0·26 mole) in ether (500 ml.) was added dropwise (3 hr.) with stirring. A few minutes later the solution became colourless. It was allowed to warm to room temperature, kept overnight, decanted from a trace of " polymethylene," and fractionally distilled, to give silicon tetrachloride (31 g., 38%), b. p. 56—58°, and trichlorochloromethylsilane (13 g., 46%), b. p. 112—113°.

(*b*) By the same procedure, but at −78°, silicon tetrachloride (27%) and trichlorochloromethylsilane (46%) were obtained.

(*c*) By the same procedure as under (*b*), in the presence of copper bronze, silicon tetrachloride (34·5%) and trichlorochloromethylsilane (62%) were obtained.

(*d*) To a solution of silicon tetrachloride (74 g., 0·435 mole) in ether (100 ml.) at −78° were added boron trifluoride (1 ml. of N-ether solution), and then diazomethane (9·5 g., 0·225 mole) in ether (500 ml.) (1 hr.). The reaction was vigorous and " polymethylene " (1·9 g., 63%) was precipitated. The filtrate yielded silicon tetrachloride (57 g., 77%), but no trichlorochloromethylsilane.

(*e*) To a solution of silicon tetrachloride (84 g., 0·49 mole) in *n*-pentane (100 ml.) at −50° was added dropwise (3 hr.) with stirring diazomethane (6·9 g., 0·165 mole) in *n*-pentane (500 ml.). Reaction was very slow, with formation of a white precipitate. After a further 3 hr. at −50°, the solution was allowed to warm to room temperature, kept for 3 days, and then filtered with exclusion of moisture. " Polymethylene " (1·85 g., 80%) was obtained. The filtrate yielded silicon tetrachloride (66 g., 79%) but no trichlorochloromethylsilane.

[9] Gilman and Dunn, *Chem. Rev.*, 1953, **52**, 77.
[9] Pritchard and Skinner, *ibid.*, 1955, **55**, 745.
[10] Lang, *Ber.*, 1888, **21**, 1580; Cox, Sharratt, Wardlaw, and Webster, *J.*, 1936, 129.
[11] Karrer, Wehrli, Biedermann, and Vedova, *Helv. Chim. Acta*, 1928, **11**, 233.
[12] Shaw, Thesis, London, 1955; *J.*, 1956, 2779; Hughes, personal communication; Eaborn, personal communication.
[13] Arndt, *Org. Synth.*, 1947, Coll. Vol. II, p. 165.

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Reaction of trimethylchlorosilane with 9-diazofluorene. (*a*) Excess of trimethylchlorosilane (2·5 ml.) in ether (10 ml.) was added to 9-diazofluorene [14] (0·78 g.) in ether (50 ml.). No apparent reaction occurred. After 1 hr. copper bronze (0·05 g.) was added; nitrogen evolution then lasted for 1 hr. After a further 2 hr., the solution was filtered, and the filtrate concentrated to give deep orange-red needles of di-9-fluorenylidene (0·28 g., 43%), m. p. and mixed m. p. 189—190°.

(*b*) Trimethylchlorosilane (2·5 g., 0·023 mole) was distilled into a solution of 9-diazofluorene (3·0 g., 0·0156 mole) in pure, dry pyridine (50 ml.). Copper bronze (0·5 g.) was added. Gas evolution occupied 24 hr., and the solution became dark. It was kept at room temperature for 72 hr. Decantation left a mixture of purple and blue crystals. Extraction with boiling benzene removed the purple compound, which on recrystallisation from the same solvent gave purple fluorenone azine (0·11 g., 4%), m. p. and mixed m. p. 271—272°. Blue dichroic needles of dipyridinocupric chloride (1·1 g., 48%) remained (Found: N, 9·6; Cl, 24·45; Cu, 21·4. Calc. for $C_{10}H_{10}N_2Cl_2Cu$: N, 9·6; Cl, 24·2; Cu, 21·7%). Optical, morphological, and *X*-ray examinations (for which we thank Dr. C. H. Carlisle) show that they are identical with a specimen prepared according to directions by Cox *et al.*[10]

The author is grateful to Professor W. Wardlaw, C.B.E., D.Sc., for his encouragement.

BIRKBECK COLLEGE, MALET STREET, LONDON, W.C.1. [*Received, October 12th,* 1956.]

[14] Schönberg, Awad, and Latif, *J.*, 1951, 1368.

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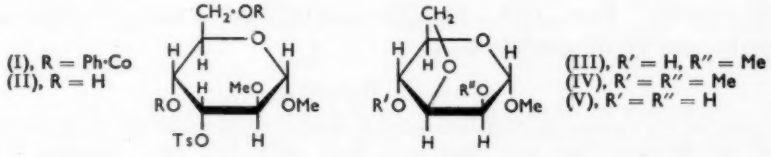
547. *Methyl* 3 : 6-*Anhydro*-2-O-*methyl*-α-D-"*altropyranoside*" (-*mannopyranoside*).

By A. B. FOSTER.

THE action of methanolic sodium methoxide on methyl 4 : 6-di-*O*-benzoyl-2-*O*-methyl-3-*O*-toluene-*p*-sulphonyl-α-D-altropyranoside (I) has been reported [1] to yield methyl 3 : 6-anhydro-2-*O*-methyl-α-D-altropyranoside. Reactions which involve the formation of anhydro-rings from toluene-*p*-sulphonyl derivatives usually occur with Walden inversion at the carbon atom which carries the toluene-*p*-sulphonyloxy-residue.[2] Further, a study of models shows that only four methyl 3 : 6-anhydro-D-hexopyranosides are structurally possible and these have the galactose,[3] glucose,[4] mannose,[5] and talose configurations of which only the latter is unknown. It was therefore predicted and proved that the "3 : 6-anhydro-D-altroside" derivative was in fact methyl 3 : 6-anhydro-2-*O*-methyl-α-D-mannopyranoside (III).



Treatment of methyl 2-*O*-methyl-3-*O*-toluene-*p*-sulphonyl-α-D-altropyranoside (II) with methanolic sodium methoxide gave methyl 3 : 6-anhydro-2-*O*-methyl-α-D-mannopyranoside (III) which on methylation with sodium, methyl iodide, and liquid ammonia yielded crystalline methyl 3 : 6-anhydro-2 : 4-di-*O*-methyl-α-D-mannopyranoside (IV).

[1] Robertson and Whitehead, *J.*, 1940, 319.
[2] Peat, *Adv. Carbohydrate Chem.*, 1946, **2**, 37.
[3] Haworth, Jackson, and Smith, *Nature*, 1938, **42**, 1075; *J.*, 1940, 620.
[4] Haworth, Owen, and Smith, *J.*, 1941, 88.
[5] Valentin, *Coll. Czech. Chem. Comm.*, 1934, **6**, 354.

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An identical product was obtained on methylation of methyl 3 : 6-anhydro-α-D-mannopyranoside (V). There can be little doubt about the structure of the latter compound which is usually prepared by the action of alkali on 6-halogeno-6-deoxy, or 6-toluene-*p*-sulphonyl derivatives of methyl α-D-mannopyranoside.[5-7]

Experimental.—Methyl 3 : 6-*anhydro*-2-*O*-*methyl*-α-D-*mannopyranoside.* A solution of methyl 2-*O*-methyl-3-*O*-toluene-*p*-sulphonyl-α-D-altropyranoside {2 g., m. p. 117—118°, $[\alpha]_D$ +87° (*c*, 1·28 in $CHCl_3$). Robertson and Whitehead [1] quote m. p. 118°, $[\alpha]_D$ +88·1° in $CHCl_3$, for this compound} in methanol (60 ml.) in which sodium (0·3 g.) had been dissolved was boiled under reflux for 5 hr. Thereafter the solution was diluted with water (60 ml.), neutralised with dilute sulphuric acid, and evaporated under diminished pressure. The residue was extracted with hot chloroform (100 ml.), the extract dried ($MgSO_4$) and evaporated, and the solid residue recrystallised from chloroform–ether, giving methyl 3 : 6-anhydro-2-*O*-methyl-α-D-mannopyranoside (0·29 g., 28%) in prisms, m. p. 105—106°, $[\alpha]_D$ +103° (*c*, 1·5 in $CHCl_3$). Robertson and Whitehead [1] report m. p. 107—108°, $[\alpha]_D$ 105·1° in $CHCl_3$, for the product obtained by the action of alkali on methyl 4 : 6-di-*O*-benzoyl-2-*O*-methyl-3-*O*-toluene-*p*-sulphonyl-α-D-altropyranoside.

Methyl 3 : 6-*anhydro*-2 : 4-*di*-*O*-*methyl*-α-D-*mannopyranoside.* (*a*) Methyl 3 : 6-anhydro-2-*O*-methyl-α-D-mannopyranoside (1·02 g.) was added during 1 hr. to liquid ammonia (30 ml.), in which sodium (0·4 g.) had been dissolved. Methyl iodide (4 ml.) was then added during 30 min. (vigorous mechanical agitation was maintained throughout) and after a further 30 min. the ammonia was evaporated and the residue extracted several times with ether. Evaporation of the combined extracts and crystallisation of the residue from ether at −30°, with seeding, gave methyl 3 : 6-anhydro-2 : 4-di-*O*-methyl-α-D-mannopyranoside (0·5 g., 43%) as square plates, m. p. 31—32°, $[\alpha]_D$ +104·1° (*c*, 1·4 in H_2O) (Found : OMe, 46·2. $C_9H_{16}O_5$ requires OMe, 45·6%). Robertson and Whitehead obtained this compound as a syrup, $[\alpha]_D$ +69° (in $CHCl_3$).

(*b*) Methyl 3 : 6-anhydro-α-D-mannopyranoside (1·35 g., prepared by Dr. W. J. G. Jones) was methylated as in (*a*) to yield a di-*O*-methyl derivative (1·15 g., 73%), m. p. 32—33°, $[\alpha]_D$ +101·2° (*c*, 1·0 in H_2O) (Found : OMe, 46·4%). The m. p. of a mixture with the product from (*a*) was 31—32°.

The author thanks Professor F. Smith and Professor M. Stacey, F.R.S., for their interest.

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EDGBASTON, BIRMINGHAM, 15. [*Received, December 27th*, 1956.]

[6] Haskins, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1946, **88**, 628.
[7] Foster, Overend, Stacey, and Vaughan, *J.*, 1954, 3367.

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548. *The Use of Equilibrium Constants to calculate Thermodynamic Quantities. Part III.* Equilibria in the System* tert.*-Butyl Bromide–*iso*Butene–Hydrogen Bromide.*

By K. E. HOWLETT.

EQUILIBRIA in the gaseous system *tert.*-butyl bromide–*iso*butene–hydrogen bromide were studied by Kistiakowsky and Stauffer.[1] This work has been repeated because discrepancies had been found between our earlier results [2] and those of Kistiakowsky and Stauffer for the corresponding chloride system.

Experimental.—The technique is described in Part I.[2] Glass wool is a satisfactory catalyst for attainment of equilibrium in the decomposition of *tert.*-butyl bromide. *tert.*-Butyl bromide was prepared by Bryce-Smith and Howlett's method [3] and had b. p. 72·8°, f. p. −16·3°, n_D^{25}

* Part II, *J.*, 1955, 1784.

[1] Kistiakowsky and Stauffer, *J. Amer. Chem. Soc.*, 1937, **59**, 165.
[2] Howlett, *J.*, 1951, 1409.
[3] Bryce-Smith and Howlett, *J.*, 1951, 1141.

1·4249. It was stored in the dark at −80° when not being distilled into the reaction chamber. In order to obviate errors arising from pressure measurements on non-ideal gases, all experiments were made at pressures of 40—90 mm. at 100—210°. Under these conditions differences between fugacities and pressures are within experimental error. To facilitate comparison with the earlier work,[1] the newly observed equilibrium constants (Table 1) are calculated in atm. units, by considering *tert.*-butyl bromide to be the product of reaction.

TABLE 1.

Temp.	99·7°	100·3°	110·4°	131·5°	155·5°	210·4°
Mean K_p (atm.$^{-1}$) *	883	843	441	110	28·1	3·14
Mean error (No. of expts. in parentheses)	12(8)	14(3)	6(5)	1·6(5)	0·1(3)	0·06(3)

* Since K_p varies in a logarithmic manner with T, the mean values of K_p were obtained by averaging $\log_{10} K_p$ at each temperature.

In the *tert.*-butyl bromide–*iso*butene–hydrogen bromide system, our results agree closely with those of Kistiakowsky and Stauffer. The combined results can therefore be summarised by the method detailed in " Handbuch der Physik " [4] in the form

$$\log_{10} K_p = (18850 \pm 140)/4{\cdot}575T - (8{\cdot}12 \pm 0{\cdot}06)$$

Thus ΔH_{415} is 18,850 cal. mole^{-1} and ΔS_{415} is 37·14 where 415° K is the mean temperature at which observations were made. By combining ΔH with $\Delta H_f°_{415}$ for hydrogen bromide * (−8·40 kcal. mole^{-1}) and $\Delta H_f°_{415}$ for *iso*butene [5] (−4·93 kcal. mole^{-1}), $\Delta H_f°_{415}$ for *tert.*-butyl bromide is calculated to be −32·18 kcal. mole^{-1}. Similarly, by combining ΔS_{415} with $S°_{415}$ for hydrogen bromide [6] (49·78) and $S°_{415}$ for *iso*butene [7] (78·19), $S°_{415}$ for *tert.*-butyl bromide is found to be 90·83.

Sheppard [8] has assigned the fundamental vibration frequencies (excluding internal rotational modes) for *tert.*-butyl bromide, and Williams and Gordy [9] have deduced from its microwave absorption a value for the two (equal) large moments of inertia (I_B and I_C) of the molecule. The other moment (I_A) was calculated in Part II. From the results the statistical entropy of the rigid molecule can be calculated and hence the entropy due to hindered rotation (S_{hr}) may be deduced by comparison with the value 90·83 obtained above. This entropy can be used in conjunction with the reduced moment of inertia (I_m) of each methyl group and Pitzer and Gwinn's tables [10] to determine the potential (V) hindering free rotation of each methyl group. The relevant figures are: Moments of inertia (g. cm.^{2} × 10^{40}): I_A, 185·0; I_B, 412·1; I_C, 412·1; I_m, 5·251: Entropy components at 415° K: S_v 13·77; S_{t+r} 68·33; $S°$ 90·83; S_{hr} 8·73; V = 3100 cal. mole^{-1}. The

TABLE 2. *Entropies, specific heats, and heats of formation in the gas phase.*

Temp. (K)	298·16°	400°	500°	600°	700°
$S°$	80·52	89·55	97·77	105·4	112·5
$C_p°$	27·88	34·15	39·48	43·97	47·78
$\Delta H_f°$ (kcal. mole^{-1})	−30·48	−31·99	−33·09	−33·88	−34·43

value of the hindering potential is clearly of the correct order of magnitude. It has therefore been used in the calculation of some of the thermodynamic functions for *tert.*-butyl bromide over the temperature range 298—700° K (see Table 2).

Further, as indicated in Part II, the results can be used to deduce a value

* The value appropriate to 25° given by Partington (" An Advanced Treatise on Physical Chemistry," Longmans, London, 1949), corrected by means of Kirchhoff's equation.

[4] " Handbuch der Physik," Springer, Berlin, 1928, Vol. 3, Chap. 13.
[5] Kilpatrick, Prosen, Pitzer, and Rossini, *J. Res. Nat. Bur. Stand.*, 1946, **36**, 559.
[6] Gordon and Barnes, *J. Chem. Phys.*, 1933, **1**, 692.
[7] Kilpatrick and Pitzer, *J. Res. Nat. Bur. Stand.*, 1946, **37**, 163.
[8] Sheppard, *Trans. Faraday Soc.*, 1950, **46**, 527.
[9] Williams and Gordy, *J. Chem. Phys.*, 1950, **18**, 994.
[10] Pitzer and Gwinn, *ibid.*, 1942, **10**, 428.

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of 59·6 kcal. mole^{-1} at 25° for the bond dissociation energy of the C–Br bond in *tert.*-butyl bromide; and comparison with the data for the rate constants for unimolecular decomposition [11] of *tert.*-butyl bromide gives the rate constants for homogeneous bimolecular addition of hydrogen bromide to *iso*butene to be $k = 10^{7.4} \exp(-24{,}000/RT)$ l. mole^{-1} sec.$^{-1}$

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[11] Harden and Maccoll, *J.*, 1955, 2454.

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549. *Chromatography of Polynitronaphthylamines.*

By E. R. WARD and P. R. WELLS.

LARSON and HARVEY [1] found that mixtures of nitroanilines and mixtures of certain isomeric substituted nitroanilines could be separated quantitatively by chromatography. Hunter [2] (cf. Larson and Harvey [1]) suggested that these results could be explained in relation to the possibility of the occurrence of intramolecular hydrogen bonding, and the relative stability of the resulting structure. As Hoyer [3] found, among isomers the one which can form a chelated hydrogen-bonded structure is most weakly adsorbed.

We now find that this method, with minor modifications, can be applied successfully to the separation of mixtures of di- and/or tri-nitronaphthylamines, but fails with all mixtures of mononitronaphthylamines so far examined (cf. Dean,[4] and Ward and Coulson [5]). Mixtures of related compounds, *e.g.*, 7-nitro-1-naphthylamine and 2 : 4-dibromo-7-nitro-1-naphthylamine, have also been so separated. Most of our mixtures arose from the hydrolysis of nitrated *N*-acylnitronaphthylamines and the method has made it possible to determine the relative proportions of isomers arising in such nitrations. Furthermore we have separated completely mixtures which contain one or more isomers in relatively small concentration, *e.g.*, that of dinitronaphthylamines arising from the mononitration of *N*-acetyl-3-nitro-2-naphthylamine. Since the hydrolysis product invariably contains appreciable amounts of side-products (in the case of hydrolysed-polynitro-*N*-phthaloylnaphthylamines possibly half the material) two chromatographic treatments are usually required, the first removing side-products (which are usually much more strongly adsorbed) and crudely separating the mixture, the second yielding pure nitro-amines. The separations of polynitronaphthylamines are much facilitated by there usually being appreciable differences in the colours of the products.

Although we agree with Hunter [2] that chelation is a major factor we also find that others must be taken into account. Thus separations 1, 2, 3, and 11 are explained completely by chelation (steric inhibition of chelation intervening in 11) but against this there is the outstanding case of the failure to separate the chelated 2-nitro-1-naphthylamine from the non-chelated 4-nitro-1-naphthylamine. Furthermore the chelated 1 : 6-dinitro-2-naphthylamine (separation 7) is more strongly adsorbed than the two 6 : *x*-dinitro-2-naphthylamines which cannot possibly be more chelated and are almost certainly not chelated. Solubility differences should account for the separation of dinitronaphthylamines from trinitronaphthylamines (separations 8, 9, and 10) and must certainly intervene in other cases (*e.g.*, 14). Separations 4, 6, and 12 might be explained by differences in basicity, chelation effects being absent or being taken as equivalent. In separation 5 it

[1] Larson and Harvey, *Chem. and Ind.*, 1954, 45.
[2] Hunter, "Progress of Stereochemistry," Butterworths, London, 1954, Vol. 1, p. 232.
[3] Hoyer, *Z. Electrochem.*, 1950, **54**, 413.
[4] Dean, Thesis, London, 1952.
[5] Ward and Coulson, *J.*, 1954, 4541.

is reasonable to assume that the least strongly adsorbed compound, 1 : 3-dinitro-2-naphthylamine, is the most strongly chelated of the three and that the other dinitronaphthylamines are separable by virtue of differences in basicity.

Experimental.—General procedure. The method followed was largely that of Larson and Harvey. The hydrolysed nitration products were usually dissolved in benzene but, where they were not readily soluble, mixtures of benzene and ethyl acetate were employed, thus restricting the volume of the initial solution. The columns were developed to produce separate coloured bands with benzene or benzene–ethyl acetate in varying proportions, each band was then separately eluted in several fractions with similar solvents (the concentration of ethyl acetate usually being progressively increased according to the observed rate of elution). The composition of each fraction was judged by the colour of the solid obtained by evaporation, m. p., and mixed m. p. Where required selected fractions were bulked together and rechromatographed to give a complete separation. In one case satisfactory elution was obtained with benzene–ethanol but in general ethanol was not a satisfactory eluant since it tended to elute side-products which normally remained at the top of the column with the alternative solvents. As frequently reported,[1, 4, 6] we found acetone to be an unsatisfactory solvent.

No.	Mixture in order of elution			Ratio *	Solvents † Orig.	Develop.	Eltn.
1	2 : 5-$(NO_2)_2$-1	4 : 5-$(NO_2)_2$-1		1 : 2	C 3 : 1	C 3 : 1	C 1 : 1, B
2	2 : 7-$(NO_2)_2$-1	4 : 7-$(NO_2)_2$-1		1 : 2	A	D 4 : 1	D 4 : 1, D 4 : 1
3	3 : 8-$(NO_2)_2$-1	3 : 5-$(NO_2)_2$-1		1 : 1	A	C 9 : 1	C 9 : 1, C 3 : 2
4	3 : 8-$(NO_2)_2$-2	3 : 5-$(NO_2)_2$-2		1 : 1	C 9 : 1	C 6 : 1	C 4 : 1, C 1 : 1
5	1 : 3-$(NO_2)_2$-2	3 : 8-$(NO_2)_2$-2	3 : 6-$(NO_2)_2$ 2	15 : 3 : 2	A	A	A; C 8 : 1, C 5 : 1; B
6	4 : 8-$(NO_2)_2$-2	4 : 5-$(NO_2)_2$-2		1 : 1	C 6 : 1	C 3 : 1	C 1 : 1, C 1 : 1
7	6 : *x*-$(NO_2)_2$-2 ‡	6 : *y*-$(NO_2)_2$-2	1 : 6-$(NO_2)_2$-2	2 : 1 : 9	C 9 : 1	C 3 : 1	C 3 : 1, C 3 : 1, C 3 : 1
8	2 : 5-$(NO_2)_2$-1	2 : 4 : 5-$(NO_2)_3$-1		1 : 1	C 2 : 1	C 2 : 1	C 2 : 1, C 2 : 1
9	2 : 7-$(NO_2)_2$-1	2 : 4 : 7-$(NO_2)_3$-1		3 : 4	A	A	C 4 : 1, C 2 :1
10	2 : 7-$(NO_2)_2$-1	4 : 7-$(NO_2)_2$-1	7 : *x* : *x*-$(NO_2)_3$-1 §	1 : 4 : 4	C 9 : 1	C 9 : 1	C 9 : 1, C 9 : 1, C 3 : 1
11	1 : 3 : 5-$(NO_2)_3$-2	1 : 3 : 8-$(NO_2)_3$-2		19 : 16	A	C 9 : 1	C 9 : 1, C 4 : 1
12	1-Br-3-$(NO_2)_2$-2	3-$(NO_2)_2$-2		1 : 1	A	A	C 8 : 1, C 5 : 1
13	2 : 4-Br_2-7-(NO_2)-1	7-(NO_2)-1		7 : 1	A	C 9 : 1	C 9 : 1, C 9 : 1
14	1-Br-3-(NO_2)-2	1 : 6-Br_2-3(NO_2)-2		1 : 1	A	A	A, C 4 : 1

* Approximate ratio of components of mixture as isolated from the column.

† A Benzene, B ethyl acetate, C benzene–ethyl acetate in proportions (v/v) indicated, D benzene–ethanol. The eluting solvents are given in the order in which they eluted the respective amines.

‡ *x* and *y* are probably 4 or 8. § Probably 4 : 5 : 7-trinitro-1-naphthylamine.

The following mixtures of nitronaphthylamines could not be separated: 2-nitro-1-naphthylamine and 4-nitro-1-naphthylamine, 5-nitro-2-naphthylamine and 8-nitro-2-naphthylamine, 3-nitro-1-naphthylamine and 4-nitro-2-naphthylamine. *N*-Acetyl-2 : 3-dinitro-1-naphthylamine could not be separated from *N*-acetyl-3 : 4-dinitro-1-naphthylamine, but 3 : 4-dinitro-1-naphthylamine and *N*-acetyl-2 : 3-dinitro-1-naphthylamine were readily separated.

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[6] Fuhrmann, *J. Recherches Centr. nat. Recherche sci., Labs Bellevue (Paris)*, 1953, No. 25, pp. 257, 258; *Chem. Abs.*, 1954, **48**, 7983.

550. 2-*Acetamido*-2-*deoxy*-D-*galactitol* ("N-*Acetyl*-D-*galactosaminol*").

By W. R. C. Crimmin.

This note records the preparation and characterisation of 2-acetamido-2-deoxygalactitol (*N*-acetylgalactosaminol), which was required as a reference compound in structural studies of oligosaccharides derived from blood-group mucopolysaccharides.[1] 2-Acetamido-2-deoxy-D-sorbitol (*N*-acetyl-D-glucosaminol) was prepared by catalytic hydrogenation of 2-acetamido-2-deoxy-α-D-glucopyranose [2] but the corresponding aminodeoxygalactitol has not been described. Sodium borohydride [3] was used for reduction of 2-acetamido-2-deoxy-α-D-galactopyranose; the crystalline galactitol was isolated in reasonable yield and was further characterised as the penta-*O*-acetyl derivative.

Experimental.—*2-Acetamido-2-deoxy-D-galactitol.* Sodium borohydride (0·5 g.) in water (20 ml.) was added slowly with occasional shaking to 2-acetamido-2-deoxy-α-D-galactopyranose (0·8 g.) in water (15 ml.) at 0°. The mixture was kept at 0° for 30 min. and at room temperature for 2 hr. Excess of borohydride was then destroyed with 4N-hydrochloric acid. The solution was concentrated *in vacuo* and the borate removed as the methyl ester by distillation.[4] The residue was dissolved in water, and de-ionised with Biodeminrolite resin (carbonate form). The solution was again concentrated, and the residue crystallised from water–acetone (1 : 1 v/v) by addition of light petroleum to incipient crystallisation. The product (400 mg.) had m. p. 174—176°, $[\alpha]_D = -42°$ (*c* 0·353 in H_2O) (Found: C, 42·8; H, 7·7; N, 6·2. $C_8H_{17}O_6N$ requires C, 43·0; H, 7·7; N, 6·3%). Paper chromatographic analysis in pyridine–ethyl acetate–water–acetic acid (5 : 5 : 3 : 1 v/v) showed a single component having the same R_P value as 2-acetamido-2-deoxygalactopyranose and a positive reaction to periodate–benzidine [5] reagent but a negative one to benzidine [6] and ninhydrin [7] reagents.

Penta-O-acetyl derivative. 2-Acetamido-2-deoxygalactitol (80 mg.) was acetylated with sodium acetate–acetic anhydride. Crystallisation from methanol gave *2-acetamido-1 : 3 : 4 : 5 : 6-penta-O-acetyl-2-deoxy-D-galactitol* (60 mg.), m. p. 176—178°, $[\alpha]_D = +15°$ (*c* 0·532 in $CHCl_3$) (Found: *O*-acetyl,[8] 49·7. $C_{18}H_{27}O_{11}N$ requires 49·7%).

Hydrochloride. The galactitol (50 mg.) in N-hydrochloric acid (6·5 ml.) was heated in a sealed ampoule for 5 hr. The solution was taken to dryness and gave an uncrystallisable syrup, $[\alpha]_D = -9°$ in water. Chromatographic analysis on paper showed a single component having the same R_P value as 2-amino-2-deoxygalactose hydrochloride; while giving positive reactions to periodate–benzidine, ninhydrin, and silver nitrate–sodium hydroxide [9] reagents the hydrochloride was negative to aniline–diphenylamine [10] reagent.

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[*Received, February 1st*, 1957.]

[1] Côté and Morgan, *Nature*, 1956, **178**, 1171.
[2] Karrer and Meyer, *Helv. Chim. Acta*, 1937, 20, 626.
[3] Whelan and Morgan, *Chem. and Ind.*, 1955, 1449.
[4] Khym, Zill, and Cheniae, *J. Amer. Chem. Soc.*, 1953, **75**, 1339.
[5] Cifonelli and Smith, *Analyt. Chem.*, 1954, **26**, 1132.
[6] Bacon and Edelman, *Biochem. J.*, 1951, **48**, 114.
[7] Toennies and Kola, *Analyt. Chem.*, 1951, **23**, 823.
[8] Wolfrom, Konigsberg, and Soltzberg, *J. Amer. Chem. Soc.*, 1936, **58**, 490.
[9] Trevelyan, Proctor, and Harrison, *Nature*, 1950, **166**, 444.
[10] Buchan and Savage, *Analyst*, 1952, **77**, 401.

551. *Influence of* ortho-*Substituents on the Stretching Frequencies of Side-chain Carbonyl Groups in Substituted Benzenes.*

By D. G. O'Sullivan and P. W. Sadler.

Nucleophilic reactions, and certain other properties, of the side chain of a substituted benzene are influenced by *meta*- or *para*-substituents in a manner which can be related to the σ-values [1] of the latter substituents. The effect of an *ortho*-substituent is complicated, steric and field factors being superimposed, to varying extents, on polar effects. Attempts to determine polar effects of *ortho*-substituents, and consequently to assess the magnitude of other influences producing specific *ortho*-effects, always involve the adoption of some basic assumption which, although plausible, is never certain. Thus McDaniel and Brown [2] assumed that proton-acceptance by certain substituted pyridines provides a nearly ideal reference system for the estimation of purely polar contributions of *ortho*-substituents, and Taft,[3] following earlier work by Ingold,[4] assumed that the ratio of rate constants of base- to acid-catalysed hydrolysis of benzoic esters depends on polar factors only.

A simple connection often exists between certain infrared frequencies and polar effects.[5] Carbonyl frequencies are linearly dependent on the σ-values of *meta*- and *para*-substituents in benzenoid compounds,[6] and parallel monotonic sequences with σ-values also exist for

Substituent factors and carbonyl frequencies [a] (*cm.*$^{-1}$) *of* ortho-*substituted benzenoid compounds.*

Subst.	NH_2	Me	H	F	I	Br	Cl	CF_3	NO_2
σ_p [1]	−0·660	−0·170	0·0	0·062	0·276	0·232	0·227	0·551	0·778
pK_a [b]	6·68	5·97	5·17	−0·44	1·82	0·90	0·72	—	—
E_σ [c]	—	0·0	—	—	0·38	0·38	0·37	—	0·95
E_s [d]	—	0·0	—	—	−0·20	0·01	0·18	—	−0·71
σ [e]	—	−0·080	0·0	—	—	—	0·325	—	0·650
Benzoic acids	1673	—	1706	1708	1712	1713	1713	—	1719
Acetanilides	—	1683	1685	—	1693	—	1694	—	1703
Hydroxyiminoacetanilides	—	1678	1680	1681	1682	1683	1683	1686	1685
Anthranilic acids	—	—	1673	—	1700	1700	1692	—	—
Isatins (β-CO group) [f]	—	1731	1740	—	1741	1745	1745	1750	—
,, (α-CO group) [g]	—	1755	1755	1755	1761	1763	1765	1768	1772

[a] In chloroform. [b] Values for pyridines.[2] [c] Taft polar factors.[3] [d] Taft steric factors.[3] [e] Mamalis and Rydon σ-values.[9] [f] Substituent in position 4. [g] Substituent in position 7.

the stretching frequencies of the amino-, hydroxy-, and nitro-groups.[7] Although the number of compounds listed is small, the data presented in the annexed Table indicate a regularity in the frequency patterns for various series of *ortho*-substituted benzenoid compounds. The magnitudes of the frequency shifts [ν(subst.) − ν(unsubst.)] depend on the basic structures as follows: hydroxyiminoacetanilides < isatins (β-CO frequencies) < benzoic acids < acetanilides, isatins, (α-carbonyl frequencies) < anthranilic acids. Effects of *ortho*- as well as *meta*- and *para*-substituents can be transmitted through an NH group attached to a benzene ring.[8]

[1] Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 188; Jaffé, *Chem. Rev.*, 1953, **53**, 191.
[2] McDaniel and Brown, *J. Amer. Chem. Soc.*, 1955, **77**, 3757.
[3] Taft, *ibid.*, 1952, **74**, 3122; 1953, **75**, 4231.
[4] Ingold, *J.*, 1930, 1032.
[5] Bellamy, *J.*, 1955, 4221.
[6] Flett, *Trans. Faraday Soc.*, 1948, **44**, 767; Davison, *J.*, 1951, 2456; Fuson, Josien, and Shelton, *J. Amer. Chem. Soc.*, 1954, **76**, 2526; O'Sullivan and Sadler, *J.*, 1956, 2202; Kellie, O'Sullivan, and Sadler, *J.*, 1956, 3809.
[7] Ingraham, Corse, Bailey, and Stitt, *J. Amer. Chem. Soc.*, 1952, **74**, 2297; Kross and Fassel, *ibid.*, 1956, **78**, 4225.
[8] O'Sullivan and Sadler, *J. Org. Chem.*, 1956, **21**, 1179.

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The Table shows that the frequencies increase with increasing *para*-σ-values. The fluoro-substituent spoils an otherwise possible correlation with the pK's of pyridine bases.[2] In general, the shifts increase with increase in Taft's polar-displacement constants for *ortho*-groups,[3] but the relation is not linear. No correlation exists with Taft's steric parameters.[3]

Approximate linear dependence exists between the frequency shifts and the σ-values for *ortho*-groups suggested by Mamalis and Rydon.[9] The latter values were obtained from rate measurements on the alkaline hydrolysis of substituted benzoyloxyethyldimethylsulphonium iodides, and specific *ortho*-effects are reputed to be absent as the point of attack is well removed from the benzene ring. Good internal correlations exist between the infrared data of the different series. Thus plotting frequency shifts for acetanilides, hydroxyiminoacetanilides, and isatins against those of benzoic acids provides sets of points that lie on, or close to, a family of straight lines, one for each series of compounds. The results presented here are too limited to warrant statistical treatment, but suffice to suggest that more searching investigations might provide a useful reference system for the general study of *ortho*-effects.

Experimental.—In each series of compounds, the spectra were determined consecutively, under identical conditions, by using a Perkin-Elmer 21 double-beam recording spectrometer fitted with a rock-salt prism.

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[9] Mamalis and Rydon, *Nature*, 1950, **166**, 404.

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552. *The H_0 Acidity Scale in Aqueous Perchloric Acid.*

By T. G. BONNER and J. C. LOCKHART.

ALTHOUGH aqueous perchloric acid is readily available in concentrations up to 72% w/w, the H_0 acidity function has not been measured above 64% $HClO_4$. Hammett and Deyrup [1] did not proceed beyond this point because of the danger of explosion; they also found that some indicators, which were stable in concentrated sulphuric acid, decomposed irreversibly in solutions of perchloric acid.

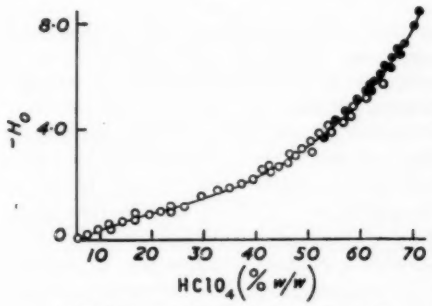
2 : 4-Dinitro-1-naphthylamine is not attacked by perchloric acid up to 72% concentration and is thus a suitable indicator for extending the H_0 scale. Indicators which had to be rejected were benzylideneacetophenone, which decomposed on irradiation with the ultraviolet light used in the spectrophotometric analysis of its solutions, and 2 : 4-dinitrodiphenylamine which, although behaving normally in concentrated sulphuric acid to give a pale yellow solution, appeared to decompose in perchloric acid, to a deep brown solution similar to that reported [1] for 4-nitrodiphenylamine.

The indicator base used by Hammett and Deyrup in their region of highest acidity was 2 : 4-dinitroaniline, but few measurements were reported for it. It has now been more extensively investigated over the range 50—62% $HClO_4$, and a new pK_a value (−4·36) evaluated for it on the basis of Hammett's pK_a value of −3·18 for 2 : 4-dichloro-6-nitroaniline.[1,2] The measurements of the ionisation ratios [B]/[BH$^+$] now reported for 2 : 4-dinitroaniline and 2 : 4-dinitro-1-naphthylamine permit the calculation of accurate values of the acitity function H_0 over the range 50—71% $HClO_4$ from the usual equation $H_0 = pK_a + \log [B]/[BH^+]$, where [B] and [BH$^+$] represent the concentrations of the un-ionised

[1] Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1932, **54**, 2721.
[2] Hammett and Paul, *ibid.*, 1934, **56**, 827.

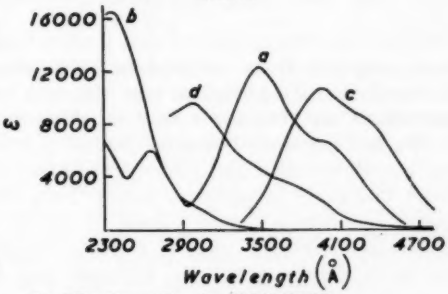
and ionised forms of the indicator in a medium of acidity H_0, and K_a the acidity constant of the acid BH^+. These values are given in the Table. Fig. 1 shows that H_0 values for acids

FIG. 1.



○ Data from Hammett and Deyrup.[1]
● Present work.

FIG. 2.



a 2 : 4-Dinitroaniline in 45·6% $HClO_4$.
b 2 : 4-Dinitroaniline in 70·0% $HClO_4$.
c 2 : 4-Dinitro-1-naphthylamine in 44·2% $HClO_4$.
d 2 : 4-Dinitro-1-naphthylamine in 72·0% $HClO_4$.

stronger than 61% perchloric acid form a curve continuous with that previously reported for acids below this strength.

2 : 4-Dinitroaniline ($pK_a = -4.36$)			2 : 4-Dinitro-1-naphthylamine ($pK_a = -6.37$)			2 : 4-Dinitro-1-naphthylamine ($pK_a = -6.37$)		
$HClO_4$ (%)	log [B]/[BH^+]	$-H_0$	$HClO_4$ (%)	log [B]/[BH^+]	$-H_0$	$HClO_4$ (%)	log [B]/[BH^+]	$-H_0$
49·6	1·27	3·09	59·6	1·25	5·12	67·3	−0·60	6·97
50·3	0·80	3·56	61·4	0·90	5·47	67·5	−0·69	7·06
53·0	0·55	3·81	62·0	0·84	5·53	68·3	−0·87	7·24
54·2	0·31	4·05	62·7	0·58	5·79	70·2	−1·58	7·95
55·5	0·04	4·32	64·0	0·25	6·12	71·3	−2·09	8·46
57·2	−0·28	4·64	65·0	−0·03	6·40			
59·5	−0·78	5·14	65·3	−0·05	6·42			
62·2	−1·25	5·61	66·4	−0·39	6·76			

Experimental.—Materials. 2 : 4-Dinitroaniline was crystallised from alcohol to a constant spectrum, $\varepsilon_{max.} = 12{,}300$ at 3480 Å in dilute aqueous perchloric acid ($\varepsilon_{max.} = 12{,}800$ at 3480 Å has been reported in aqueous sulphuric acid [3]), and had m. p. 180°. 2 : 4-Dinitro-1-naphthylamine was prepared by nitration of acetnaphthalide in acetic acid and hydrolysis of the dinitro-derivative.[4] The brown product was boiled with charcoal and crystallised from alcohol to a constant spectrum, $\varepsilon_{max.} = 10{,}600$ at 3960 Å in dilute aqueous perchloric acid; it had m. p. 244°.

Absorption spectra. These were measured on a Hilger " Uvispek " spectrophotometer and the indicator ionisation ratio was obtained from the equation $[B]/[BH^+] = (\varepsilon_{BH^+} - \varepsilon)/(\varepsilon - \varepsilon_B)$, where ε_{BH^+} and ε_B are the extinction coefficients at any selected wavelength of the ionised and un-ionised forms of the indicator respectively, and ε is the extinction coefficient at the same wavelength for a particular medium containing the concentrations [B] and [BH^+] of the two forms. The absorption spectra of the ionised and un-ionised forms of 2 : 4-dinitroaniline and 2 : 4-dinitro-1-naphthylamine in perchloric acid are shown in Fig. 2. As the absorption curves were very slightly displaced to higher wavelengths with increasing acidity of the media, [B]/[BH^+] was calculated at several different wavelengths on either side of the peak, and the mean value taken.

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[*Received, February 14th*, 1957.]

[3] Bartlett and McCollum, *ibid.*, 1956, **78**, 1441.
[4] Morgan and Evens, *J.*, 1919, 1126.

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553. 2-*Nitro*-1-*naphthoic Acid.*

By R. D. Topsom and J. Vaughan.

2-Nitro-1-naphthaldehyde and 2-nitro-1-naphthoic acid, previously unreported, have been prepared from 2-nitro-1-methylnaphthalene *via* 2-nitro-1-naphthylpyruvic acid. 2-Nitro-1-methylnaphthalene was obtained by Veselý *et al.*[1] in low yield by a lengthy procedure; we obtained it by a satisfactory 3-stage process.

We first prepared 4-bromo-1-methylnaphthalene in 28% yield from 1-methylnaphthalene by sulphonation and subsequent bromination, reported[2] to be desirable in order to avoid unwanted by-products arising from direct bromination.[3,4] We found, however, that a commercial " pure " grade of 1-methylnaphthalene on direct bromination, gave an almost theoretical yield of 4-bromo-derivative. This was nitrated at the 2-position and then debrominated by Edwards and Stewart's method.[5] Attempts to oxidise 1-methyl-2-nitronaphthalene gave mixtures of polycarboxylic acids; however, condensation with a large excess of ethyl oxalate at $<0°$ gave the potassium derivative of ethyl 2-nitro-1-naphthylpyruvate, and oxidation of the derived acid gave a mixture of 2-nitro-1-naphthaldehyde and 2-nitro-1-naphthoic acid. This hindered acid was purified by taking advantage of its resistance to esterification. It may be esterified through its silver salt but fails to yield an anilide by the normal method.

In the condensation with ethyl oxalate under reflux in the absence of a large excess of ester, the main product was 1 : 2-di-(2-nitro-1-naphthyl)ethane (cf. ref. 6).

In other methods investigated, 2-nitro-1-bromonaphthalene failed to react with a Grignard reagent and with *n*-butyl-lithium, and oxidation of 3-nitroacenaphthene gave only very low yields of 2-nitronaphthalic acid, making subsequent mercuration and decarboxylation impracticable.

Experimental.—*4-Bromo-1-methylnaphthalene.* Bromine (38 ml.) in carbon tetrachloride (200 ml.) was added during 2 hr. at $-7°$ to a stirred solution of 1-methylnaphthalene (100 g. of Light's " pure ") in carbon tetrachloride (250 ml.) containing small amounts of iron powder and iodine. Stirring was continued for a further 1 hr. at $-7°$ and the mixture was then left for 2 hr. as the temperature rose. Excess of bromine was removed by treatments with 2N-sodium hydroxide and with water. Solvent was removed at atmospheric pressure and a fraction, b. p. 179—180°/27 mm., was collected. Redistillation gave 4-bromo-1-methylnaphthalene (145 g., 93%), b. p. 170—171°/20 mm.

4-Bromo-1-methyl-2-nitronaphthalene. The method of Veselý *et al.*[7] gave variable yields, the best (*ca.* 35%) being obtained by addition of nitrating acid to 4-bromo-1-methylnaphthalene. The 2-nitro-product was obtained as pale yellow crystals, m. p. 122° after repeated recrystallisation from light petroleum (b. p. 60—80°) and ethanol.

1-Methyl-2-nitronaphthalene. 4-Bromo-1-methyl-2-nitronaphthalene (10 g.), cuprous oxide (7·5 g.), acetic anhydride (5·2 ml.), and dry, freshly distilled pyridine (40 ml.) were refluxed for 1·5 hr., then poured into 5% acetic acid (500 ml.). After 12 hr. the solid was filtered off and extracted with light petroleum (5 × 100 ml.; b. p. 60—80°). Removal of solvent yielded crystals, which were further extracted with light petroleum, then recrystallised twice from ethanol. The 1-methyl-2-nitronaphthalene was obtained as yellow crystals (4·0 g. 57%), m. p. 56°.

2-Nitro-1-naphthylpyruvic acid. A solution of potassium ethoxide [from potassium (2·5 g.), ethanol (10 ml.), and ether (10 ml.)] was added at 0° to stirred, freshly distilled diethyl oxalate

[1] Veselý, Štursa, Olejníček, and Rein, *Coll. Czech. Chem. Comm.*, 1929, **1**, 493.
[2] Fieser and Steligman, *J. Amer. Chem. Soc.*, 1939, **61**, 137.
[3] Mayer and Sieglitz, *Ber.*, 1922, **55**, 1835.
[4] Robinson and Thompson, *J.*, 1932, **135**, 2015.
[5] Edwards and Stewart, *Chem. and Ind.*, 1952, 472.
[6] Mayer and Oppenheimer, *Ber.*, 1916, **49**, 2137.
[7] Veselý, Štursa, Olejníček, and Rein, *Coll. Czech. Chem. Comm.*, 1930, **2**, 145.

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(75 ml.). After 15 min. 2-nitro-1-methylnaphthalene (11·5 g.) was added with stirring, during 30 min. at 0°. Stirring was continued for 30 min. and the mixture then kept at −10° for 24 hr. Filtration and washing with chilled ether gave the potassium derivative of *ethyl 2-nitro-1-naphthylpyruvate* as a deep red solid. Treatment for 12 hr. with 0·5N-hydrochloric acid (250 ml.), filtration, and two recrystallisations from ethanol afforded the light yellow ester (11 g., 62%), m. p. 110·5° (Found: C, 63·0; H, 4·65; N, 5·0. $C_{15}H_{13}O_5N$ requires C, 62·7; H, 4·5; N, 4·9%).

The ester (5 g.) was stirred into a warm solution of potassium hydroxide (1 g.) in dry ethanol (30 ml.). After dissolution of solid material, water (200 ml.) was added and after 2 hr. the mixture was acidified with dilute hydrochloric acid. Filtration and two recrystallisations from 30% aqueous acetic acid furnished yellow *2-nitro-1-naphthylpyruvic acid* (3·8 g.), m. p. 179° (Found: C, 60·9; H, 3·6; N, 5·4. $C_{13}H_9O_5N$ requires C, 60·2; H, 3·5; N, 5·4%).

Oxidation. The acid (3 g.) was dissolved in a solution of sodium hydroxide (0·96 g.) in water (120 ml.). To this stirred solution was added, during 10 min., a solution of potassium permanganate (2·4 g.) in water (250 ml.) and stirring was continued for 30 min. Manganese dioxide was removed and the supernatant liquid was acidified before extraction with ether. Extraction of the ether layer with sodium hydrogen carbonate solution and acidification of this gave crude 2-nitro-1-naphthoic acid (1·5 g.), m. p. 120—130°. The solid from evaporation of the ether layer was recrystallised (charcoal) from light petroleum (b. p. 60—80°) and twice recrystallised from methanol, to give *2-nitro-1-naphthaldehyde* (0·5 g., 21%) as yellow needles, m. p. 119° (Found: C, 65·9; H, 3·6; N, 6·9. $C_{11}H_7O_3N$ requires C, 65·7; H, 3·5; N, 7·0%). The *semicarbazone* had m. p. 279° (Found: N, 21·5. $C_{12}H_{10}O_3N_4$ requires N, 21·7%).

The crude acid was refluxed for 4 hr. in ethanol (20 ml.) under a constant stream of dry hydrogen chloride. Charcoal was added before filtration and the residue from the evaporated filtrate was taken up in ether. Extraction with sodium hydrogen carbonate and acidification gave the still impure acid (1·0 g.), m. p. 187—195°. Extraction with hot 30% aqueous ethanol and three recrystallisations from 30% ethanol then gave pure, pale yellow *2-nitro-1-naphthoic acid* (0·6 g., 24%), m. p. 202° (Found: C, 61·0; H, 3·3; N, 6·3. $C_{11}H_7O_4N$ requires C, 60·8; H, 3·25; N, 6·45%). The pale yellow *ethyl ester*, obtained from the silver salt and ethyl iodide and purified by recrystallisation from ethanol, had m. p. 92° (Found: C, 63·4; H, 4·8; N, 5·8. $C_{13}H_{11}O_4N$ requires C, 63·6; H, 4·5; N, 5·7%).

2-Nitro-1-naphthoic acid was also obtained in 50% yield (m. p. 199°) from the aldehyde by oxidation with potassium permanganate in aqueous acetone.

1 : 2-Di-(2-nitro-1-naphthyl)ethane. 2-Nitro-1-methylnaphthalene (3 g.) and diethyl oxalate (2 ml.) were added to a solution of sodium ethoxide (from 0·75 g. of sodium in 20 ml. of ethanol). After 20 minutes' refluxing, the mixture was added to water (100 ml.). The solid was washed with hot ethanol, and two recrystallisations from chlorobenzene furnished *1 : 2-di-(2-nitro-1-naphthyl)ethane* (1·5 g.) as bright yellow flakes, m. p. 232° (Found: C, 70·9; H, 4·5; N, 7·5. $C_{22}H_{16}O_4N_2$ requires C, 70·9; H, 4·3; N, 7·5%), insoluble in most common organic solvents.

We acknowledge the help of Mr. F. R. H. Gerhard in the initial work on 2-nitro-1-methylnaphthalene. Analyses were carried out in the microanalytical laboratory (Dr. A. D. Campbell) of the University of Otago.

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[*Received, February 25th,* 1957.]

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554. *The Pyrolysis of Hexafluoroethane.*

By P. D. MERCER and H. O. PRITCHARD.

THE possibility has been explored of obtaining a pyrolytic value for the dissociation energy $D(CF_3{-}CF_3)$; this quantity is still not known with any accuracy.[1-3] Hexafluoroethane was pyrolysed in a flow system with toluene in the usual way,[4] in the temperature range

[1] Dibeler, Reese, and Mohler, *J. Res. Nat. Bur. Stand.*, 1956, **57**, 113.
[2] Farmer, Henderson, Lossing, and Marsden, *J. Chem. Phys.*, 1956, **24**, 348.
[3] Pritchard, Pritchard, Schiff, and Trotman-Dickenson, *Chem. and Ind.*, 1955, 896.
[4] Clark and Pritchard, *J.*, 1956, 2136.

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846—1019°. The upper part of this range represents the limit of the toluene-carrier technique because of the difficulty of removing toluene decomposition products from the reaction vessel at sufficient speed and because of the deposition of coke in the reaction zone and tar in the exit tube. Two sets of experiments were performed in which different methods of analysis were employed to determine the ratio of CF_3H : C_2H_6 in the products: infrared absorption spectrometry and mass spectrometry. The measurements were made on the fraction which was involatile at −195° but volatile at −80°; however, with mass-spectrometric analysis, a much more careful sampling was necessary because butadiene and/or butenes were formed (from the toluene) which interfered with the peak at 51 used for the estimation of CF_3H, and a further distillation at about −165° to −170° was necessary to prevent this interference. The results from both sets of measurements were the same: the rate constant for the decomposition $C_2F_6 \longrightarrow 2CF_3\cdot$ up to 960°, was $k \approx 10^8 \exp(-50{,}000/RT)$ sec.$^{-1}$ after which it became apparently independent of temperature. The reaction is probably heterogeneous, but we could not test this by packing the vessel because it is difficult to maintain a free flow of gas through the restricted space in the packed zone; but even if the reaction were to prove homogeneous, one could not regard the observed activation energy as a measure of the dissociation energy in view of the abnormal frequency factor with which it is associated.

As an alternative approach, it would be interesting to compare the decompositions of $PhCH_2$–CH_3 and $PhCF_2$–CF_3, which would not involve such high temperatures, but it is not feasible [5] to make the latter substance in sufficient quantities; some experiments with its precursor $PhCCl_2\cdot CF_3$ yielded no relevant information since the initial process apparently involved the fission of a C–Cl bond (substantial quantities of hydrogen chloride were produced). We conclude therefore that the pyrolytic approach to the C–C dissociation energy in hexafluoroethane is unsuitable, although more information on the nature of its pyrolysis might be obtained by using methane instead of toluene as a carrier gas.

UNIVERSITY OF MANCHESTER. [*Received, February 28th*, 1957.]

[5] Simons and Herman, *J. Amer. Chem. Soc.*, 1943, **65**, 2064.

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